EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	0	copolymer and "vp:stma"	USPAT; EPO; DERWENT	AND	ON	2007/04/26 17:51
L2	8	copolymer and vp same stma	USPAT; EPO; DERWENT	AND	ON	2007/04/26 17:52
L3	2	("6132705").URPN.	USPAT	AND	ON	2007/04/26 17:55
L4	2	("6132705").URPN.	USPAT	AND	ON	2007/04/26 18:02
L5	5484	copolymer and vinylpyrrolidone same acrylate	USPAT; EPO; DERWENT	AND	ON	2007/04/26 18:03
L6	755	5 and membrane	USPAT; EPO; DERWENT	AND	ON	2007/04/26 18:03
L7	99	6 and polysulphone	USPAT; EPO; DERWENT	AND	ON	2007/04/26 18:04
L8	1	7 and 210/500.41.ccls.	USPAT; EPO; DERWENT	AND	ON	2007/04/26 18:04
L9	2	("5376274" | "5543465").PN. OR ("6113785").URPN.	US-PGPUB; USPAT; USOCR	AND	ON	2007/04/26 18:47
L10	2	("5376274" | "5543465").PN. OR ("6113785").URPN.	US-PGPUB; USPAT; USOCR	AND	ON	2007/04/26 18:56
L11	0	("6113785").URPN.	USPAT	AND	ON	2007/04/26 18:56
L12	0	("6113785").URPN.	USPAT	AND	ON	2007/04/26 18:57
L13	0	("6113785").URPN.	USPAT	AND	ON	2007/04/26 18:57
L14	2	("5376274" | "5543465").PN.	US-PGPUB; USPAT; USOCR	AND	ON	2007/04/26 18:59
L15	413	210/500.41.ccls.	USPAT; EPO; DERWENT	AND	ON	2007/04/26 19:02
L16	60	polysulfone and n-vinylpyrrolidone same copolymer and hydrophobic and hydrophilic	USPAT; EPO; DERWENT	AND	ON	2007/04/26 19:05
L17	35	16 and membrane	USPAT; EPO; DERWENT	AND	ON	2007/04/26 19:33

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TITLE: Filter medium having a limited surface negative charge for treating a blood material

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****See application file for complete search history****

REF-CITED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL		
4046720	September 1977	Rembaum et al.	N/A	N/A	N/A
4604208	August 1986	Chu et al.	N/A	N/A	N/A
4880548	November 1989	Pall et al.	N/A	N/A	N/A
4888115	December 1989	Marinaccia et al.	210/636	N/A	N/A
4936998	June 1990	Nishimura et al.	210/502.1	N/A	N/A
5021160	June 1991	Wolpert	N/A	N/A	N/A
5051185	September 1991	Watanabe et al.	502/403	N/A	N/A
5286449	February 1994	Kuroda et al.	210/490	N/A	N/A

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
0341413	November 1989	EP	
0397403	November 1990	EP	
1249063	October 1989	JP	
3502094	May 1991	JP	
2061812	May 1981	GB	
8903717	May 1989	WO	

ART-UNIT: 136
PRIMARY-EXAMINER: Dawson; Robert A.
ASSISTANT-EXAMINER: Walker; W. L.
ATTY-AGENT-FIRM: Birch, Stewart, Kolasch & Birch

ABSTRACT:

Disclosed is a filter medium for treating a blood material selected from the group consisting of a leukocyte-containing suspension and plasma, comprising a polymeric, porous element having, in a surface portion thereof, a negative charge and having a surface electric charge of not smaller than -30 .mu.eq/g of the polymeric, porous element. The filter medium and an apparatus having the filter medium packed in a casing having an inlet and an outlet, can be advantageously used for treating a blood material, for example, for separating leukocytes from a leukocyte-containing suspension including whole blood, for blood dialysis or for removing undesired proteinous substances and the like from whole blood or plasma by adsorption-filtration, while effectively controlling a concentration of bradykinin (which is causative of anaphylactic reactions) in a treated blood to a level not exceeding 4,000 pg/ml.

34 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Brief Summary Text - BSTX (9):

In the fields of blood filtration, blood dialysis, plasma separation, plasma component filtration and the like, there are used **membrane** type filter media, such as hollow fiber **membranes,** flat **membranes,** or the like which are made of regenerated cellulose, polyacrylonitrile, polymethyl methacrylate, **polysulfone,** polyolefins, cellulose acetate and the like.

Brief Summary Text - BSTX (16):

It is still another object of the present invention to provide a filter **membrane** free of the bradykinin problem, for use in separating an undesired substance from whole blood or plasma.

Brief Summary Text - BSTX (23):

The terminology "filter medium" used herein collectively means a medium for use in fractionating whole blood or for use in separating at least one blood or plasma component, a contaminant, or a foreign substance, by contacting a blood material with the medium, in which utilization is made of fractionation by size difference, dialysis, cohesion or sticking; adsorption by a physical or chemical action (such as electrostatic or **hydrophobic** action), or by biological interaction; or combinations thereof.

Brief Summary Text - BSTX (25):

(1) A filter medium for use in removing, separating or recovering at least one substance selected from the group consisting of at least one preselected blood component (e.g., leukocytes, platelets or blood aggregates), a substance foreign to blood components (e.g., tissue pieces, broken bone pieces, broken pieces of a device) and a mixture thereof from a blood material. This type of filter medium comprises a polymeric, porous element selected from a filter fabric, such as a woven fabric, a non-woven fabric, a cotton fabric or the like; a porous article, such as a sponge; and a porous **membrane**. Another type of filter medium can be mentioned, for example, beads or a hollow fiber, onto which a monoclonal antibody or the like is immobilized in order to specifically separate a specific leukocyte fraction. This type of filter medium is also included in this category (1).

Brief Summary Text - BSTX (26):

(2) A filter medium for use in separating whole blood into a blood cell product and plasma, or for use in separating whole blood or plasma, each containing at least one preselected substance, into the at least one preselected substance and the remaining whole blood or plasma substantially free of the at least one preselected substance. This type of filter medium is a porous **membrane** capable of separating substances by a molecular size difference between the substances. This type of filter medium is used for separating various undesired substances from plasma for treating patients suffering from

renal failure by extracorporeal circulation of blood, for example, separating low molecular weight proteins by haemofiltration, or separating other low molecular weight components of plasma, such as electrolytes, urea, creatinine and the like by haemodialysis. This type of filter medium is also used for collecting or separating plasma from whole blood to conduct plasma pheresis or produce plasma products, or for fractionating plasma components, e.g., separation of macroglobulin and immune complex from albumin. Examples of porous **membranes** include hollow fiber porous **membranes** and flat porous **membranes,** each having a vast plurality of through-pores.

Brief Summary Text - BSTX (27):

(3) A filter medium for use in separating whole blood or plasma, each containing at least one preselected substance, into the at least one preselected substance and a remaining whole blood or plasma substantially free of the at least one preselected substance by adsorption-filtration. This type of filter medium comprises a polymeric, porous element comprised of an adsorptive composite. The adsorptive composite comprises a polymeric, porous substrate having, on a surface thereof including pore surfaces, functional groups capable of selectively binding the above-mentioned at least one preselected substance thereto. Examples of adsorptive composites include beads having polyanions immobilized thereon; **hydrophobic** resin; porous beads having immobilized thereon a saccharide, an amino acid, or an oligomer or polymer thereof; porous beads having immobilized thereto an antibiotic or other pharmaceutical substances; and those which are obtained by substituting fibrous materials for the substrate beads of the above-mentioned bead composites. This type of filter medium is used for removing, separating, or collecting plasma proteins, such as cholesterol, an autoantibody, an immune complex, a bilirubin, a **hydrophobic** amino acid, a proteinous pharmaceutical substance, and the like; or plasma components, such as a lipid, an amino acid, a nucleic acid, a low molecular weight compound, and the like.

Brief Summary Text - BSTX (43):

With respect to the method for measuring surface electric charges of the filter media of categories (1) and (2), the above-mentioned salt-splitting, neutralization titration method is not suitable because these filter media have relatively small specific surface areas (generally less than 5 m.sup.2 /g). Examples of suitable porous elements for filter media of category (1) include woven fabrics, non-woven fabrics and sponge, and Examples of suitable porous elements for filter media of category (2) include porous **membranes,** such as hollow fiber porous **membranes** and flat porous **membranes**. As a result of the investigations by the present inventors, it has been found that the surface electric charges of the polymeric, porous elements for the filter media of categories (1) and (2) can be easily determined by a so-called iodide method, in which iodine is reacted with iodide ions in an organic solvent, such as an alcohol, in the presence of the polymeric, porous

element having a negative charge, wherein a negative charge (when only a negative charge is present) or an apparent negative charge (as a balance between the positive and negative charges when both positive and negative charges are present) functions as a catalyst, so that the reaction proceeds to form triiodide complex ions depending on the quantity of the negative charge, and the amount of the thus formed triiodide complex ions is measured by absorption spectrometry to thereby determine the quantity of the negative charge or apparent negative charge on the surface of the polymeric, porous element. When the surface of the polymeric, porous element exhibits an apparent positive charge as a balance between the positive and negative charges, the above-mentioned reaction for forming triiodide complex ions does not proceed, so that confirmation can be made at least with respect to the fact that the polymeric, porous element has a surface electric charge of not smaller than -30 .mu.eq/g.

Brief Summary Text - BSTX (65):

In addition to the negative functional groups, positive functional groups and/or nonionic functional groups may coexist at or on a surface portion of the filter medium. Examples of nonionic functional groups include: nonionic **hydrophilic** functional groups, such as a hydroxyl group, a polyethylene glycol chain, an amide group (such as dimethylamide group, diethylamide group or diisopropylamide group), an aromatic polyester chain (such as a polyethylene terephthalate chain or polybutylene terephthalate chain), an aliphatic polyester chain, a polyether chain (such as methylene glycol or propylene glycol) and a polycarbonate chain, which are effective for improving **hydrophilic** properties of the filter medium; and nonionic **hydrophobic** functional groups, such as an alkyl group, a fluoroalkyl chain, and an allyl chain, which are effective for imparting **hydrophobic** properties to the filter medium. Although any functional groups of the above examples can coexist in the filter medium, nonionic **hydrophilic** functional groups or chains having these **hydrophilic** groups are preferred because those groups or chains have excellent effects especially on filter media for removing leukocytes.

Brief Summary Text - BSTX (79):

Any method of the above five methods can be employed in the present invention. A preferred method varies depending on the type and application of the filter medium. However, in general, the method for coating the filter medium surface with a compound or a polymer having **hydrophilic,** neutral or positive functional groups, is practically preferred because it is the easiest method.

Brief Summary Text - BSTX (87):

Examples of materials to be used for preparing polymeric, porous element of the filter medium of the present invention include polyesters, such as polyethylene terephthalate,

polybutylene terephthalate and polyoxyethylene terephthalate; polyacrylonitrile; polyamides, such as nylon 6 and nylon 6, 6; aromatic polyamide; polystyrene and derivatives thereof; polyolefins, such as polyethylene, polypropylene and polybutene; polymeric compounds which are obtained by polymerization of methacrylate derivatives, such as methyl methacrylate and ethylmethacrylate; polymeric compounds which are obtained by polymerization of acrylate derivatives, such as methyl acrylate and ethyl acrylate; polymeric compounds, such as polytrifluorochloroethylene, polyvinyl formal, **polysulfones,** polyurethanes, polyvinyl acetal and polycarbonates; homopolymers, copolymers, or block copolymers of the above-mentioned polymeric compounds, a blend or alloy thereof; cellulose and/or a cellulose derivative; regenerated fibers; a blend or alloy of regenerated fibers with the above-mentioned synthetic, polymeric compounds.

Brief Summary Text - BSTX (94):

Other methods for attaining a specific, limited surface electric charge of the porous element of the filter medium of the present invention include amidation in which a known carbodiimide, such as dicyclohexylcarbodiimide, is reacted with a compound, such as primary and secondary amines, or a compound having an amino group, and esterification, such as methylesterification by employing diazomethane. Examples of esterification and amidation agents include dicyclohexylcarbodiimide (DCC), diazomethane, dialkyl sulfate and alkyl halide. The agents are not limited to the above examples. Still other methods for attaining a specific, limited surface electric charge in the surface portion of porous element of the filter medium of the present invention include esterification, in which the porous element is reacted with hydroxyl groups within the element by subjecting it to dehydrating treatment while heating under vacuum; embedding of negative groups into the porous element by contacting with **hydrophobic** surfaces thereof; and surface modification of the porous element by graft copolymerization which employs a conventional technique, such as radiation and plasma treatment.

Brief Summary Text - BSTX (95):

It is also possible to attain a specific, limited surface electric charge of the porous element, i.e., in the range of not smaller than -30 .mu.eq/g of the element by a method in which the element is coated with a **hydrophilic** polymer not having a negative charge or a nitrogen-containing positive polymer.

Brief Summary Text - BSTX (100):

However, for example, by causing neutral **hydrophilic** groups to be retained at or on the surface of the porous element, the CWST value can be increased while keeping a surface electric charge in the range of not smaller than -30 .mu.eq/g of the porous element.

Brief Summary Text - BSTX (148):

In another form of the filter medium of the present invention, the filter medium used in separating whole blood into a blood cell product and plasma, or in separating whole blood or plasma, each containing at least one preselected substance, into the at least one preselected substance and the remaining whole blood or plasma product substantially free of the at least one preselected substance. The filter medium comprises a polymeric, porous element having, in a surface portion thereof, a negative charge and having a surface electric charge of not smaller than -30 .mu.eq/g of the polymeric, porous element, wherein the polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 ~~/mmHg.~~

Brief Summary Text - BSTX (149):

There are various types of **membrane** filter media having various quantities of negative charges in their surface portions. The present inventors have conducted measurements of the quantities of negative charges in their surface portions, and found that all of the measured conventional hollow fiber porous **membranes** and flat porous **membranes,** which are made mainly of polyacrylonitrile, cellulose, polymethylmethacrylate or the like, have a negative charge of greater than -50 .mu.eq/g (namely, for example, -53 .mu.eq/g, -55 .mu.eq/g or so), since a negative charge has been intentionally introduced to their surface portions for improving the wettability of the **membrane** to blood.

Brief Summary Text - BSTX (150):

A porous **membrane** having a negative charge in a surface portion thereof of greater than -50 .mu.eq/g of the medium causes the problem that the quantity of bradykinin is largely increased in the surface portion thereof. As mentioned above, it has been found that with respect to the kinin problem, the higher the surface electric charge of the **membrane,** the better the removal of the kinin problem. Furthermore, a porous **membrane** having a positive charge at or on the portion thereof in a large amount causes no problem with respect to the increase of kinin.

Brief Summary Text - BSTX (151):

However, as a result of the investigations by the present inventors, it has been found that it is not necessarily advantageous to completely remove the negative functional groups present at or on the surface portion of a porous **membrane,** because in practical use the presence of negative functional groups is important in improving the wettability of the surface of the porous **membrane** to blood. It is especially important to increase the

electric charge in the surface portion of the porous **membrane** without reducing the hydrophilicity thereof.

Brief Summary Text - BSTX (152):

That is, a porous **membrane** which has a surface electric charge of not smaller than -30 .mu.eq/g of the **membrane** is excellent and particularly preferred from the viewpoint of the kinin problem as well as wettability to blood.

Brief Summary Text - BSTX (153):

Examples of materials to be used for preparing the **membrane** type filter medium of the present invention include polyacrylonitrile; cellulose; cellulose acetate; **polysulfone**; polyvinyl alcohol; copolymers of vinyl alcohol and ethylene; cuprammonium regenerated cellulose; polyesters, such as polyethylene terephthalate, polybutylene terephthalate and polyoxyethylene terephthalate; polyamides, such as nylon 6 and nylon 6, 6; aromatic polyamide; polystyrene and derivatives thereof; polyolefin, such as polyethylene, polypropylene and polybutene; polymeric compounds which are obtained by polymerization of methacrylate derivatives, such as methyl methacrylate and ethyl methacrylate; polymeric compounds which are obtained by polymerization of acrylate derivatives, such as methyl acrylate and ethyl acrylate; polymeric compounds such as polytrifluorochloroethylene, polyvinyl formal, polyurethane, polyvinyl acetal and polycarbonate; a homopolymer, copolymer, or block copolymer of the above-mentioned polymeric compound, a blend thereof, or an alloyed product thereof; regenerated cellulose and/or a cellulose derivative; regenerated fibers; or a blend or alloyed product of regenerated fibers with the above-mentioned synthetic, polymeric compound.

Brief Summary Text - BSTX (154):

Of the above-mentioned materials, particularly preferred are a polymeric compound made mainly of polyacrylonitrile; a homopolymer or copolymer which is obtained by polymerization of methacrylate derivatives, such as methyl methacrylate and ethyl methacrylate; and a polymeric compound made mainly of regenerated cellulose and/or a cellulose derivative, from the viewpoint of fabricatability into a porous **membrane** and the sharpness of the pore distribution of the resultant porous **membrane**.

Brief Summary Text - BSTX (155):

The surface of the **membrane** type filter medium comprising the above-mentioned material can be modified with a compound having a low or high molecular weight by conventional techniques, such as covalent bonding, ionic bonding, radiation-graft polymerization or plasma treatment, physical adsorption, embedding or precipitation immobilization. For example, there is known a conventional method in which the surface

of the filter medium is modified by conventional techniques, such as graft polymerization of polymeric compounds or monomers thereof by radiation or plasma treatment, or covalent bonding (Japanese Patent Application Laid-Open Specification Nos. 1-249063 and 3-502094). Examples of monomers and polymeric compounds for use in surface modification of the **membrane** type filter medium include vinyl monomers (for example, methacrylic acid; acrylic acid; acrylic acid or methacrylic acid derivatives such as 2-methacryloyloxyethyl succinate, mono (2-acryloyloxyethyl) acid phosphate, 2-sulfoethyl methacrylate and 2-methacryloyloxyethyl phthalate; styrene derivatives, such as p-styrene sulfonic acid and p-vinylbenzoic acid; and phenol derivatives such as vinylphenol); allyl compounds, such as sodium allyl sulfonate; acetylene derivatives; polymeric compounds which are obtained by polymerization of monomers, such as trioxane derivatives having negative groups; and copolymers and block copolymers of the above monomers with acrylic and methacrylic esters having a polymerizable functional group (preferably a vinyl group or an acetylene group), such as 2-hydroxyethyl methacrylate, 2-hydroxyethyl acrylate, 1,2-dihydroxyethyl methacrylate, methoxytriethyleneglycol methacrylate, methoxynonaethyleneglycol methacrylate, methyl methacrylate, ethyl methacrylate, methyl acrylate and ethyl acrylate, with neutral monomers, such as styrene and derivatives thereof, and with cationic monomers such as N,N-diethylaminoethyl methacrylate, N,N-dimethylaminoethyl methacrylate, N,N-diethylaminoethyl acrylate and N,N-dimethylaminoethyl acrylate. Of these compounds, polymeric compounds obtained by polymerization of vinyl monomers are particularly preferable, because they have a high degree of polymerization, and are easily available.

Brief Summary Text - BSTX (156):

The negative charge in the surface portion of the **membrane** type filter medium of the present invention can be reduced by using, for example, an acrylonitrile copolymer containing no electric charge as a raw material in the preparation of a porous **membrane**. Such a raw material gives a desirable hollow fiber porous **membrane** or flat porous **membrane**.

Brief Summary Text - BSTX (157):

Other methods for increasing the surface electric charge of the **membrane** type filter medium of the present invention include amidation, in which a known carbodiimide, such as dicyclohexylcarbodiimide, is reacted with a compound, such as primary and secondary amines or a compound having an amino group, and esterification, such as methylesterification by employing diazomethane. Still other methods for increasing a surface electric charge of the **membrane** type filter medium of the present invention include esterification in which the medium is reacted with hydroxyl groups within the medium by subjecting to dehydrating treatment while heating under vacuum; embedding of negative groups into the medium by contacting with **hydrophobic** surfaces thereof.

Brief Summary Text - BSTX (158):

Still other method includes surface modification of the medium by graft copolymerization which employs a conventional technique such as radiation and plasma treatment. It is also possible to increase a surface electric charge of the medium by forming, on the surface thereof, a coating layer comprising a compound having no positive or negative functional groups, and having a **hydrophilic** partial structure such as polyethylene glycol chain, or a **hydrophilic** compound having positive groups.

Brief Summary Text - BSTX (159):

The zeta-potential of a flat porous **membrane** is measured by a streaming potential measuring instrument (ZP-10B of Shimadzu Corporation, Japan).

Brief Summary Text - BSTX (160):

The zeta-potential of a hollow porous fiber is measured as follows. First, one filament of the hollow porous fiber is cut into a piece 14 cm in length to thereby obtain a sample. A platinum electrode is attached to both ends thereof, and then the fiber sample is connected through a tube to a bottle containing a potassium chloride solution having a KCl concentration of 10.sup.-3 mol/liter. To this bottle, a pressure is applied up to 0.5 kg/cm.sup.3, so that the KCl solution can pass through the hollow fiber. The streaming potential is measured, while increasing the pressure. Then, the zeta-potential is determined by the following formula. ##EQU1## Since a negative charge in the inside of a hollow porous fiber is likely to be a causative of an increase in kinin concentration in the blood material, the above-mentioned measuring method is preferable to the other method in which the entire portion of a filter medium is subjected to measurement. The zeta-potential takes a different value if the shape of surface, weight, etc. of a sample is different. Therefore, the zeta-potential of a hollow fiber porous **membrane** and that of other filter medium cannot be evaluated uniformly.

Brief Summary Text - BSTX (161):

It can be said that in one aspect, the zeta-potential represents the relationship between a hydrophilicity of the medium and a surface electric charge of the medium. Thus, the value of the zeta-potential depends on the hydrophilicity of the medium. In a hollow fiber porous **membrane,** when its zeta-potential is -2 mV or more, it can be a safe filter medium free of the bradykinin problem. When the zeta-potential becomes higher due to negative groups in the medium, the increase of bradykinin becomes smaller. Thus, the zeta potential of a hollow fiber porous **membrane** is preferably from -1 mV or more, more preferably from -0.5 to 0 mV.

Brief Summary Text - BSTX (162):

The higher the surface electric charge of the filter medium, the better the removal of the kinin problem. However, according to the study of the present inventors, it has been found that with the increase of the surface electric charge of a filter medium, the wettability of the surface of the medium is decreased to thereby increase non-specific adsorption of plasma proteins on the surface; that adhesion of platelets to the surface is increased; and that wetting of the surface is not attained easily. When the wettability of a filter medium is expressed in terms of a critical wetting surface tension (CWST), the CWST value of the **membrane** type filter medium is preferably 20 dyn/cm or more, more preferably 50 dyn/cm or more to attain favorable wetting of the medium.

Brief Summary Text - BSTX (163):

The wettability of the medium is not determined by only the quantity of negative functional groups on the surface thereof. However, in conventional porous **membranes** for treating blood material, comprising a polyacrylamide or the like, sulfonic acid groups or carboxyl groups in the pores prominently contribute to wettability. The higher the value of CWST, the higher the wettability. However, along with the increase of a CWST value of the medium, an increase of kinin is observed. Thus, in actual use of a **membrane** type filter medium, the CWST value of the medium is preferably not greater than 102 dyn/cm, more preferably not greater than 90 dyn/cm.

Brief Summary Text - BSTX (164):

However, for example, by introducing neutral **hydrophilic** groups in the surface of a porous **membrane,** the CWST value can be increased while keeping the surface electric charge not smaller than -30 .mu.eq/g of the porous **membrane**.

Brief Summary Text - BSTX (165):

The CWST value can be measured in the same manner as described hereinbefore in connection with the leukocyte-removing filter medium. With respect to a hollow fiber porous **membrane,** however, prior to the measurement, a flat hollow porous fiber assembly is formed by a method in which a plurality of hollow porous fibers are arranged and placed in parallel on a flat plate, such as a slide glass, without leaving any space between the hollow porous fibers, and their respective both ends are fixed onto the plate with a silicone adhesive or the like.

Brief Summary Text - BSTX (166):

The average pore diameter of the **membrane** type filter medium of the present invention is determined by subjecting the filter medium to scanning electron photomicrography, followed by randomly selecting 1000 or more of the pores scattering on the photomicrograph and measuring their diameters visually. Although a suitable

average pore diameter of the **membrane** type filter medium varies depending on its use, it is preferably from 10 .ANG. to 1 .mu.m, more preferably from 10 .ANG. to 0.5 .mu.m. In the case of a filtration type dialysis **membrane,** good filtration can be obtained when its average pore diameter is from 15 to 20 .ANG.. The range of pore diameters, the thickness of the porous **membrane,** and the inner and outer diameters of the hollow porous fiber are also measured visually using photomicrographs in substantially the same manner as mentioned above. It is preferred that the pore diameter be in the range from 30 to 400 .ANG.. With respect to a hollow fiber porous **membrane,** it is preferred that the inner and outer diameters of the hollow fiber and the thickness of the porous **membrane** be as small as possible, so that a greater number of the hollow porous fibers can be contained in a unit volume of a casing, providing a large porous **membrane** area. However, from the viewpoint of a desired mechanical strength of the porous **membrane,** it is preferred that the thickness of the porous **membrane** be from 5 to 200 .mu.m, the inner diameter of the hollow porous fiber from 50 to 300 .mu.m, and the outer diameter of the hollow porous fiber from 100 to 1,000 .mu.m.

Brief Summary Text - BSTX (167):

The porosity (% by volume) of the **membrane** type filter medium of the present invention can be obtained from the following formula. ##EQU2## From the viewpoint of desired filtration efficiency, it is preferred that a porosity (% by volume) of the porous **membrane** be high. However, the porosity (% by volume) is preferably from 30 to 75% from the viewpoint of mechanical strength of the porous **membrane,** more preferably from 40 to 75% from the viewpoint of mechanical strength as well as filtration efficiency.

Brief Summary Text - BSTX (168):

The water permeability of the hollow fiber porous **membrane** of the present invention is defined as the amount of water which has passed through a unit area of the porous **membrane** from the inside to the outside thereof per unit time under a specific pressure. Although a desirable water permeability varies depending on the use of a porous **membrane,** it is preferred that this value be from 3.4 to 10,000 ml/hr/m.sup.2 /mmHg, more preferably from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg. Of these **membranes, a membrane** exhibiting a high water permeability can be advantageously employed in an artificial dialyzer, etc., by virtue of the high water permeability.

Brief Summary Text - BSTX (169):

This form of the filter medium of the present invention, i.e., the **membrane** type filter medium, is packed in a casing having an inlet for blood material and an outlet for a filtrate, and can be used as an apparatus for separating whole blood into a blood cell

product and plasma, or for removing a predetermined substance, e.g. an undesired substance from whole blood or plasma.

Brief Summary Text - BSTX (171):

the filter medium comprising a polymeric, porous element having, in a surface portion thereof, a negative charge and a surface electric charge of not smaller than -30 .mu.eq/g of the polymeric, porous element, and wherein the polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg.

Brief Summary Text - BSTX (172):

The morphology of a casing in which the **membrane** type filter medium of the present invention is to be packed is not particularly limited. A casing of any morphology can be used, as long as the casing has an inlet for whole blood or plasma and an outlet for a filtrate, or an inlet and outlet for blood and a dialyzate intake and exit. Examples of casings include a conventional casing in which a flat porous **membrane** can be packed in laminated form, a circular, triangular, quadrangular, hexangular or octangular column, to which predetermined portions of a hollow fiber porous **membrane** can be fixed, and a casing in which a hollow fiber porous **membrane** is fixed only at its blood inlet and outlet in a state such that both openings and inside hollow space of the hollow porous fiber are maintained.

Brief Summary Text - BSTX (175):

The length of a casing for the **membrane** type filter apparatus of the present invention is not particularly limited. However, the length is preferably from 15 to 35 cm from the viewpoint of ease in manufacturing as well as ease in handling blood to be treated.

Brief Summary Text - BSTX (177):

The priming of the **membrane** type filter apparatus of the present invention is preferable from the viewpoint of reducing the time required before the start of the operation, as well as rendering the operation easy. It is preferred that the priming volume be from 10 ml to 4 liters, although this varies depending on the shape, size and use of the apparatus.

Brief Summary Text - BSTX (178):

When the **membrane** type filter apparatus of the present invention is actually used, there can be provided, upstream or downstream of the filter apparatus, an extracorporeal blood circulation system or a blood transfusion line comprising at least one of the

following elements: a blood bag, a blood circuit, a chamber, a clamp, a roller clamp, a drip chamber, a needle, a drip chamber provided with mesh, a tube for a blood pump, etc.

Brief Summary Text - BSTX (180):

The **membrane** type filter medium of the present invention packed in a casing can be used for haemodialysis, filtration dialysis, separation of whole blood into plasma and a blood cell product, double filtration, concentration of a body fluid, e.g. a serous fluid from an abdominal dropsy patient, push and pull blood filtration, etc.

Brief Summary Text - BSTX (229):

Of these, a homopolymer or **copolymer** of vinyl compounds is most preferred because a negative or positive functional group can be easily introduced thereto. Representative examples of vinyl compounds include hydrocarbon compounds, such as styrene, methylstyrene, diphenylethylene, ethylethylene, dimethylstyrene, vinylnaphthalene, vinylphenanthrene, vinylmesitylene, 3,4,6-trimethylstyrene and 1-vinyl-2-ethylacetylene; styrene derivatives, such as chlorostyrene, methoxystyrene, bromostyrene, cyanostyrene, fluorostyrene, dichlorostyrene, N,N-dimethylaminostyrene, nitrostyrene, chloromethylstyrene, trifluorostyrene, trifluoromethylstyrene and aminostyrene; acrylonitrile and its derivatives, such as .alpha.-acetoxyacrylonitrile; acrylic acid and its ester, such as methyl acrylate, lauryl acrylate, chloromethyl acrylate and ethyl acetoxyacrylate; methacrylic acid and its ester, such as cyclohexyl methacrylate, dimethylaminoethyl methacrylate, glycidyl methacrylate, tetrahydrofurfuryl methacrylate and hydroxyethyl methacrylate; diethyl maleate and diethyl fumarate; vinyl ketone, such as methyl vinyl ketone and ethyl isopropenyl ketone; vinylidene compounds, such as vinylidene chloride, vinylidene bromide and vinylidene cyanide; acrylamide and its derivatives, such as methacrylamide, N-butoxymethyl acrylamide, N-phenyl acrylamide, diacetone acrylamide and N,N-dimethylaminoethyl acrylamide; vinyl derivatives of aliphatic acids, such as vinyl acetate, vinyl butyrate and vinyl caprate; thiofatty acid derivatives, such as phenyl thiomethacrylate, methyl thioacrylate and vinyl thioacetate; heterocyclic vinyl compounds, such as N-vinylsuccinimide, **N-vinylpyrrolidone,** N-vinylphthalimide, N-vinylcarbazole vinylfuran, vinylthiophene, vinylimidazole, methylvinylimidazole, vinylpyrazole, vinyloxazolidone, vinylthiazole, vinyltetrazole, vinylpyridine, methylvinylpyridine, 2,4-dimethyl-6-vinyltriazine and vinylquinoline.

Brief Summary Text - BSTX (241):

The morphology of the polymeric, porous substrate is not particularly limited. Preferred examples of morphologies include those of a sphere, a particle, a filament, a hollow fiber and a flat **membrane**. Of these, from the viewpoint of assuring a good flow of blood material through the substrate, a spherical or particulate morphology is most preferred. In the case of a spherical or particulate morphology, the porous substrate

preferably has an average particle diameter of from 10 to 10,000 .mu.m, more preferably 25 to 1,000 .mu.m, still more preferably 50 to 600 .mu.m.

Brief Summary Text - BSTX (245):

The adsorptive porous element may have a coating of a **hydrophilic** polymer which improves affinity to blood and is capable of suppressing the adhesion of platelets. In general, since blood samples are not always easily available and vary in quality, it is difficult to precisely and stably evaluate the affinity of a polymer to blood. However, the hydrophilicity of a polymer has a close correlation with the affinity thereof to blood and, therefore, its affinity to blood can be easily evaluated through the evaluation of its hydrophilicity. The hydrophilicity of a porous element can be easily evaluated, for example, by measuring the contact angle of the porous element against gas bubbles in water. In the present invention, when the adsorptive porous element is in a sheet form or a film form, the porous element preferably exhibits a contact angle of 20.degree. or more against gas bubbles in water, as measured at 25.degree. C.

Brief Summary Text - BSTX (246):

From the viewpoint of preventing the detachment of the **hydrophilic** coating from the porous substrate, it is preferred that the **hydrophilic** coating on the porous substrate be formed from a polymer. Examples of monomers which can be used for producing a **hydrophilic** polymer coating include acrylic acid, methacrylic acid and derivatives thereof, such as 2-hydroxyethyl acrylate, 2-hydroxypropyl acrylate, 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, 2-hydroxybutyl methacrylate, diethylaminoethyl methacrylate, dimethylaminoethyl methacrylate, methoxydiethylene glycol methacrylate, methoxytriethylene glycol methacrylate and glycerol monomethacrylate; methoxypolyethylene glycols, such as methoxytriethylene glycol; styrene derivatives, such as diethylaminoethyl styrene, hydroxystyrene and hydroxymethylstyrene; vinyl group-containing monomers, such as vinyl amine and vinyl alcohol; segmented polyurethane; segmented polyester; mono (2-methacryloyloxyethyl) acid phosphate; and mono (2-acryloyloxyethyl) acid phosphate. A homopolymer, a copolymer, a block copolymer and a graft copolymer and the like which are comprised of one or more of the above-mentioned monomers, may be employed for forming a coating. Also, a graft copolymer containing a monomer having a polyethylene oxide chain may be employed.

Brief Summary Text - BSTX (256):

Extracorporeal circulation of a blood material can be conducted, for example, as follows. Whole blood taken from a patient is separated into plasma and a blood cell product by a centrifugal separator or a **membrane** type plasma separator. The separated plasma is passed through the adsorber apparatus of the present invention for purification,

and then returned to the patient together with the blood cell product. Alternatively, it is possible to pass the whole blood taken from the patient through the adsorber apparatus directly for purification. Of these two methods, the former is preferred, because the flow resistance of the adsorber apparatus is smaller and a higher total adsorption capacity can be attained.

Detailed Description Text - DETX (249):

A hollow porous fiber of a PAN homopolymer, having an inner diameter of 250 .mu.m and an outer diameter of 320 .mu.m, is prepared by dry spinning. The resultant hollow porous fiber is packed in a casing having an inner diameter of 31.6 mm and a length of 210 mm, to thereby prepare a haemodialyzer as one form of the blood-treating filter apparatus of the present invention. The packing ratio and the effective **membrane** area are 68.5% and 1.0 m.sup.2 respectively Using the resultant haemodialyzer, dialysis of whole blood collected using heparin as an anticoagulant is conducted. The concentration of kinin in the treated blood taken at the blood outlet of the haemodialyzer is 750 pg/ml.

Detailed Description Text - DETX (254):

The hollow porous fiber prepared in Comparative Example 19, having an inner diameter of 250 .mu.m and an outer diameter of 320 .mu.m, is packed in a casing having an inner diameter of 31.6 mm and a length of 210 mm to thereby prepare a haemodialyzer. The packing ratio and the effective **membrane** area are 68 5% and 10 m.sup.2, respectively. Using the haemodialyzer, dialysis of whole blood collected using heparin as an anticoagulant is conducted. The concentration of kinin in the treated blood taken at the blood outlet of the haemodialyzer is 11,250 pg/ml.

Claims Text - CLTX (7):

7. The filter medium according to claim 1, for use in separating whole blood into a blood cell product and plasma or for use in separating whole blood or plasma, each containing at least one preselected substance, into said at least one preselected substance and a remaining whole blood or plasma product substantially free of said at least one preselected substance, wherein said polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg.

Claims Text - CLTX (8):

8. The filter medium according to claim 7, wherein said porous **membrane** is a hollow fiber porous **membrane** having an inner diameter of from 50 to 300 .mu.m.

Claims Text - CLTX (9):

9. The filter medium according to claim 7, wherein said polymeric, porous **membrane** comprises a material selected from the group consisting of an acrylonitrile polymer, a cellulose polymer and a methyl methacrylate polymer.

Claims Text - CLTX (27):

said filter medium comprising a polymeric, porous element having, in a surface portion thereof, a negative charge and a surface electric charge of not smaller than -30 .mu.eq/g of said polymeric, porous element, and wherein said polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg.

Claims Text - CLTX (28):

26. The apparatus according to claim 25, wherein said porous **membrane** is a hollow fiber porous **membrane** having an inner diameter of from 50 to 300 .mu.m.

Claims Text - CLTX (29):

27. The apparatus according to claim 25, wherein said **membrane** comprises a polymeric material selected from the group consisting of an acrylonitrile polymer, a cellulose polymer and a methyl methacrylate polymer.

Claims Text - CLTX (33):

31. The method according to claim 28, for use in separating whole blood into a blood cell product and plasma or for separating whole blood or plasma, each containing at least one preselected substance, into said at least one preselected substance and a remaining whole blood or plasma product substantially free of said at least one preselected substance, wherein said polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg.

Claims Text - CLTX (40):

said filter medium comprising a polymeric, porous element having, in a surface portion thereof, a negative charge and a surface electric charge of not smaller than -30 .mu.eq/g of said polymeric, porous element, and wherein said polymeric, porous element is a porous **membrane** having an average pore diameter of from 10 .ANG. to 1.0 .mu.m and having a water permeability of from 3.4 to 8,000 ml/hr/m.sup.2 /mmHg, thereby controlling a bradykinin concentration of a passed blood to a level not exceeding 4,000 pg/ml.

US-PAT-NO: 6132705

DOCUMENT-IDENTIFIER: US 6132705 A

TITLE: Cosmetic or pharmaceutical compositions for use on the skin

DATE-ISSUED: October 17, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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APPL-NO: 08/882733

DATE FILED: June 26, 1997

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	196 272 04	July 5, 1996

INT-CL-ISSUED:	[07] A61K031/215

INT-CL-CURRENT:

TYPE	**IPC DATE**
CIPS	A61 Q 1/06 20060101
CIPS	A61 Q 17/04 20060101
CIPS	A61 K 8/72 20060101
CIPS	A61 K 8/81 20060101
CIPS	A61 Q 1/02 20060101
CIPS	A61 Q 1/10 20060101
CIPS	A61 Q 19/00 20060101

US-CL-ISSUED:	424/78.02 , 424/78.03 , 424/78.06 , 526/264 , 526/303.1 , 526/328.5 , 526/329.2
US-CL-CURRENT:	424/78.02, 424/78.03 , 424/78.06 , 526/264 , 526/303.1 , 526/328.5 , 526/329.2
FIELD-OF-CLASSIFICATION-SEARCH:	526/279; 526/328.5 ; 526/329.2 ; 526/303.1 ; 526/264 ; 424/78.02 ; 424/78.03 ; 424/78.06

****See application file for complete search history****

REF-CITED:

U.S. PATENT DOCUMENTS

PAT-NO	**ISSUE-DATE**	**PATENTEE-NAME**	**US-CL**		
3808178	April 1974	Gaylord	N/A	N/A	N/A
4259467	March 1981	Keogh et al.	N/A	N/A	N/A
4661571	April 1987	Kato et al.	526/329.2	N/A	N/A
4756843	July 1988	Jarrin et al.	526/329.2	N/A	N/A
4861840	August 1989	Lim et al.	526/279	N/A	N/A
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FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
59-12907	January 1984	JP	526/329.2
2-64117	March 1990	JP	526/279
3-12416	January 1991	JP	526/279
84/00969	March 1984	WO	526/279
86/01518	March 1986	WO	526/279

OTHER PUBLICATIONS Ans 10 of 33 doc. 123:237539 in house computer searched pp. 21-24 Shinji et al. JP 07187951--950725.

ART-UNIT: 173

PRIMARY-EXAMINER: Zitomer; Fred

ATTY-AGENT-FIRM: Keil & Weinkauf

ABSTRACT:

A cosmetic or pharmaceutical composition which comprises at least one polymer or **copolymer** which is obtainable by free-radical emulsion or suspension polymerization in the presence of at least one chain-transfer reagent, has a glass transition temperature above -35.degree. C. and a content of organic volatile constituents .ltoreq.0.5% by weight, and is at least 20% by weight composed of a (meth)acrylic ester.

26 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Abstract Text - ABTX (1):

A cosmetic or pharmaceutical composition which comprises at least one polymer or **copolymer** which is obtainable by free-radical emulsion or suspension polymerization in the presence of at least one chain-transfer reagent, has a glass transition temperature above -35.degree. C. and a content of organic volatile constituents .ltoreq.0.5% by weight, and is at least 20% by weight composed of a (meth)acrylic ester.

Brief Summary Text - BSTX (1):

The present invention relates to cosmetic or pharmaceutical compositions for use on the skin, which comprise polymers or **copolymers** which are obtainable by free-radical emulsion or suspension polymerization in the presence of chain-transfer reagents to increase the water resistance.

Brief Summary Text - BSTX (4):

DE-2 833 711 describes sun screen formulations which comprise oil-soluble acrylate polymers to increase the water resistance. Both homopolymers prepared from acrylic esters and **copolymers** of acrylic esters and carboxyl-containing monomers such as (meth)acrylic acid or itaconic acid are described. The polymers are prepared without chain-transfer reagents and, in particular, by solution polymerization in a cosmetically usable oil such as isopropyl palmitate and are formulated directly in the form of the resulting solution to give a sun screen composition.

Brief Summary Text - BSTX (5):

Copolymers of N-vinylpyrrolidone and .alpha.-olefins and their use in cosmetic formulations are described, for example, in U.S. Pat. Nos. 5,219,559 and 3,423,381. They are prepared by solution polymerization without use of a chain-transfer agent and are further processed after removal of the solvent.

Brief Summary Text - BSTX (9):

We have found that this object is achieved by using (meth)acrylic ester polymers or their **copolymers** with monomers capable of free-radical copolymerization, which are obtainable by free-radical emulsion or suspension polymerization in the presence of chain-transfer reagents.

Brief Summary Text - BSTX (10):

The present invention thus relates to a cosmetic or pharmaceutical composition which comprises at least one polymer or **copolymer** which is obtainable by free-radical

emulsion or suspension polymerization in the presence of at least one chain-transfer reagent, has a glass transition temperature above -35.degree. C. (determined by DSC) and a content of organic volatile constituents .ltoreq.0.5% by weight, and is at least 20% by weight composed of a (meth)acrylic ester.

Brief Summary Text - BSTX (11):

Particularly suitable compositions are those comprising at least one polymer or **copolymer** composed of

Brief Summary Text - BSTX (20):

It is also possible to use in the composition of the polymers according to the invention water-soluble monomers which are capable of free-radical polymerization (monomers B) and which influence the physicochemical properties, such as the glass transition temperature and solubility, of the resulting **copolymer,** and the substantivity of a composition containing these polymers on the skin. They may also improve the compatibility with other components of the cosmetic or pharmaceutical preparation. Use of these monomers B in the composition of the **copolymers** according to the invention may furthermore optimize the sensation on the skin after use of the composition.

Brief Summary Text - BSTX (21):

Preferred cosmetic or pharmaceutical compositions are therefore those comprising **copolymers** composed of at least one monomer A and at least one monomer B.

Brief Summary Text - BSTX (23):

The properties of the **copolymers** which are obtained in this way and are composed of monomers A and B can be further improved by including another monomer (monomer C) which can entirely or partly replace monomer B depending on the purpose of use.

Brief Summary Text - BSTX (25):

Finally, it is possible for **copolymers** which are suitable according to the invention to contain units of another monomer (monomer D). In this case, monomers D can be copolymerized with monomers A alone or in combination with monomers B and/or C, depending on the purpose of use, for the composition of the polymers according to the invention.

Brief Summary Text - BSTX (28):

The physicochemical properties of the polymers or **copolymers** according to the invention depend on the nature of the monomers used, the relative amounts thereof and the polymerization conditions and can be specifically influenced by the choice of suitable parameters.

Brief Summary Text - BSTX (29):

The polymers according to the invention have a glass transition temperature Tg above -35.degree. C. The glass transition temperature is preferably .gtoreq.0.degree. C., and particularly preferred polymers or **copolymers** have a glass transition temperature above 35.degree. C. Polymers according to the invention with low glass transition temperatures are preferably prepared by emulsion polymerization, whereas polymers with higher glass transition temperatures are preferably obtainable by suspension polymerization. The upper limit of the glass transition temperature is generally 120.degree. C. Very particularly preferred polymers or **copolymers** have a glass transition temperature in the range from 35.degree. C. to 100.degree. C.

Brief Summary Text - BSTX (37):

The dispersions obtained by emulsion polymerization can be efficiently freed of residual monomers and other low molecular weight odorous substances which are unwanted for toxicological and olfactory reasons by passing in steam or nitrogen. These dispersions can be employed directly in the appropriate cosmetic or pharmaceutical compositions, in particular creams or lotions. The emulsion **copolymers** can, if the glass transition temperature of the polymer is sufficiently high, also be converted without difficulty by spray- or freeze-drying or else by coagulation and subsequent drying into powders which can be processed and handled very easily. These process steps make a further contribution to minimizing the content of low molecular weight volatile constituents.

Brief Summary Text - BSTX (40):

The polymers or **copolymers** described above confer increased wet substantivity on the compositions according to the invention. The compositions preferably comprise 0.2-20, in particular 0.5-10, % by weight of polymer, based on the total weight of the composition.

Detailed Description Text - DETX (3):

1. Preparation of **Copolymers** According to the Invention

Detailed Description Paragraph Table - DETL (1):

EA ethyl acrylate BA butyl acrylate EHA 2-ethylhexyl acrylate LA lauryl acrylate (C12-C14-alcohol acrylic ester) StA stearyl acrylate **StMA** stearyl methacrylate tBA t-butyl acrylate tBMA t-butyl methacrylate iBMA isobutyl methacrylate MMA methyl methacrylate **VP** vinylpyrrolidone AS acrylic acid MAS methacrylic acid NTBAM N-t-butyl acrylamide HEMA hydroxyethyl methacrylate AA acrylamide MAA methacrylamide BTCM bromotrichloromethane EHTG ethylhexyl thioglycolate ME mercaptoethanol S styrene

Detailed Description Paragraph Table - DETL (3):

TABLE 2 Exam- Monomer Chain-transfer T.sub.g ple Monomers ratio reagent [.degree. C.]
17 tBMA/LA 90/10 1.0% ME 80 18 tBMA/StA 70/30 1.5% ME 72 19 tBMA/EHA 80/20 1.2% ME 60 20 tBMA/HEMA 95/5 1.0% ME 102 21 tBMA/**VP** 95/5 0.5% ME 103 22 iBMA/**StMA** 70/30 1.5% ME 38 23 tBA/EHA/AS 80/18/2 1.2% ME 30 24 tBMA/LA/S 80/10/10 1.0% ME 82

Detailed Description Paragraph Table - DETL (5):

Parts by weight
PEG-7 hydrogenated castor oil 6.00 PEG-40 hydrogenated castor oil 0.50 PEG-45/dodecyl glycol **copolymer** 2.00 Isopropyl myristate 8.00 Liquid paraffin, high viscosity 5.00 Jojoba oil 6.00 Octyl methoxycinnamate 7.00 Benzophenone-3 2.00 Magnesium stearate 0.80 Polymer of Example 7 2.00 Preservative q.s. Magnesium sulfate.7H.sub.2 O 0.50 Glycerol 87% pure 5.00 Disodium EDTA 0.10 PEG-25 p-aminobenzoic acid 5.00 Water 50.1 Perfume oil q.s.

Claims Text - CLTX (1):

1. A cosmetic or pharmaceutical composition having an increased water resistance, and being adapted for the treatment of skin, comprising, in addition to at least one conventional cosmetic or pharmaceutical ancillary substance, an effective amount of at least one polymer or **copolymer** composed of

Claims Text - CLTX (7):

which polymer or **copolymer** is obtainable by free-radical emulsion or suspension polymerization in the presence of at least one chain-transfer reagent, and where the polymer or **copolymer** has a glass transition temperature above -35.degree. C. and a

content of organic volatile constituents .ltoreq.0.5% by weight, as a wet substantivity increasing agent.

Claims Text - CLTX (14):

8. The composition defined in claim 1, wherein the polymer or **copolymer** has a glass transition temperature >0.degree. C.

Claims Text - CLTX (17):

11. The composition defined in claim 1, wherein the polymer or **copolymer** is essentially free of low molecular weight impurities.

Claims Text - CLTX (18):

12. The composition defined in claim 1, which comprises 0.2-20% by weight, based on the total weight of the composition, of the polymer or **copolymer**.

Claims Text - CLTX (23):

17. The composition defined in claim 1, wherein the polymer or **copolymer** has a glass transition temperature >35.degree. C.

Claims Text - CLTX (25):

19. The composition defined in claim 12, which comprises 0.5-10% by weight, based on the total weight of the composition, of the polymer or **copolymer**.

Claims Text - CLTX (28):

22. A cosmetic or pharmaceutical composition having an increased water resistance, and being adapted for the treatment of skin, comprising, in addition to at least one conventional cosmetic or pharmaceutical ancillary substance, an effective amount of at least one polymer or **copolymer** composed of

Claims Text - CLTX (33):

which polymer or **copolymer** is obtainable by free-radical emulsion or suspension polymerization in the presence of at least one chain-transfer reagent, and where the polymer or **copolymer** has a glass transition temperature above -35.degree. C. and a content or organic volatile constituents .ltoreq.0.5% by weight, as a wet substantivity increasing agent.

US-PAT-NO: 6113785

DOCUMENT-IDENTIFIER: US 6113785 A

TITLE: **Polysulfone membrane** for purifying blood

DATE-ISSUED: September 5, 2000

INVENTOR-INFORMATION:

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Mukaiyama; Shigemi	Yokohama	N/A	N/A	JP

ASSIGNEE INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
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APPL-NO: 09/051335

DATE FILED: April 9, 1998

PARENT-CASE:

This application claims the benefit under 35 U.S.C. .sctn.371 of prior PCT International Application No. PCT/JP96/02940 which has an International filing date of Oct. 9, 1996 which designated the United States of America, the entire contents of which are hereby incorporated by references.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	7-286332	October 9, 1995

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/JP96/02940	October 9, 1996	WO97/13575	Apr 17, 1997	Apr 9, 1998	Apr 9, 1998

INT-CL-ISSUED: [07] A01D071/68

INT-CL-CURRENT:

TYPE	IPC DATE
CIPS	B01 D 71/00 20060101
CIPS	B01 D 67/00 20060101
CIPS	B01 D 71/68 20060101
CIPS	B01 D 71/78 20060101
CIPS	B01 D 71/80 20060101

US-CL-ISSUED: 210/500.41 , 210/500.34 , 210/500.42 , 264/41 , 264/48 , 264/49

US-CL-CURRENT: 210/500.41, 210/500.34 , 210/500.42 , 264/41 , 264/48 , 264/49

FIELD-OF-CLASSIFICATION-SEARCH: 210/500.14; 210/500.42 ; 210/500.23 ; 210/500.35 ; 210/645 ; 210/500.34 ; 264/41 ; 264/48 ; 264/49 ; 96/4

****See application file for complete search history****

REF-CITED:

U.S. PATENT DOCUMENTS

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL		
5376274	December 1994	Muller et al.	210/500.41	N/A	N/A
5543465	August 1996	Bell et al.	525/182	N/A	N/A

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
62-201603	September 1987	JP	
2-160026	February 1990	JP	

ART-UNIT: 173
PRIMARY-EXAMINER: Fortuna; Ana
ATTY-AGENT-FIRM: Birch, Stewart, Kolasch & Birch, LLP

ABSTRACT:

A **polysulfone membrane** for purifying blood having excellent compatibility with blood and the process producing the **membrane** are disclosed. The **membrane** comprises a mixed polymer phase of a graft **copolymer** and/or block **copolymer** having a molecular weight of 3.times.10.sup.5 daltons or more and comprising (A) a hydrophilic segment and (B) a hydrophobic segment (exclusive of **polysulfone**) in a total amount of from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** with the monomer unit ratio (A/B) between the segments A and B being from 0.5 to 5. The **copolymer** is preferably a graft **copolymer** where the hydrophilic segment is a polyvinylpyrrolidone segment and the hydrophobic segment is a polystyrene segment. The **membrane** can be prepared by applying a wet film formation process to a dope containing an appropriate solvent of the mixed polymer, such as N,N-dimethylacetamide. The **membrane** for purifying blood reduces cumbersomeness in the washing of the coagulated **membrane** during the film formation process and allows recovery of the solvent from the coagulating solution at a high recovery rate because the **copolymer** contained in the structure of the **membrane** is substantially not eluted into water contacted during the film formation process and the washing step.

14 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Abstract Text - ABTX (1):

A **polysulfone membrane** for purifying blood having excellent compatibility with blood and the process producing the **membrane** are disclosed. The **membrane** comprises a mixed polymer phase of a graft **copolymer** and/or block **copolymer** having a molecular weight of 3.times.10.sup.5 daltons or more and comprising (A) a hydrophilic segment and (B) a hydrophobic segment (exclusive of **polysulfone**) in a total amount of from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone**, with the monomer unit ratio (A/B) between the segments A and B being from 0.5 to 5. The **copolymer** is preferably a graft **copolymer** where the hydrophilic segment is a polyvinylpyrrolidone segment and the hydrophobic segment is a polystyrene segment. The **membrane** can be prepared by applying a wet film formation process to a dope containing an appropriate solvent of the mixed polymer, such as N,N-dimethylacetamide. The **membrane** for purifying blood reduces cumbersomeness in the washing of the coagulated **membrane** during the film formation process and allows recovery of the solvent from the coagulating solution at a high recovery rate because the **copolymer** contained in the structure of the **membrane** is substantially not eluted into water contacted during the film formation process and the washing step.

TITLE - TI (1):

Polysulfone membrane for purifying blood

Brief Summary Text - BSTX (2):

The present invention relates to a **membrane** for blood purification such as hemodialysis and hemofiltration and more specifically, the present invention relates to a **polysulfone membrane** for purifying blood having excellent compatibility with the blood and the **membrane of which the membrane** producing performance is improved in the washability of the **membrane** and recoverability of the solvent used in producing the **membrane**.

Brief Summary Text - BSTX (4):

Polysulfone resin has been extensively applied and developed as a medical material because of its excellent heat resistance, chemical resistance and .gamma.-ray resistance. The **polysulfone** resin is also used as a material in highly transmissive artificial dialyzers. However, the **polysulfone** itself is hydrophobic and exhibits poor blood compatibility by itself. Hitherto, various methods have been developed in an attempt to improve the compatibility with the blood. For example, Japanese Unexamined Patent Publication (Kokai) No. 61-93801 discloses a method of adding polyvinylpyrrolidone to

thereby improve the blood compatibility of the **membrane** and Japanese Unexamined Patent Publication (Kokai) No. 6-165926 discloses a **polysulfone** hollow fiber **membrane** containing a vinylpyrrolidone-base polymer and a polyglycol.

Brief Summary Text - BSTX (5):

The compatibility with the blood can be improved by blending a hydrophilic polymer as in these techniques, however, since the hydrophilic polymer blended with the **polysulfone** resin is water-soluble, a thorough washing of the **membrane** formed is essential. Due to this, the washing step generally takes a long time and the film formation process is inefficient. Further, when a water-soluble hydrophilic polymer is added, in addition to the problem of a cumbersome washing process, there is a serious problem in the production, due to the fact that the water-soluble polymer added during the film formation is eluted in a large amount into the coagulating solution. More specifically, at the time of recovering a solvent of the **membrane** from the coagulating solution, the solvent becomes difficult to recover because the viscosity of the coagulating solution is greatly increased due to the presence of the hydrophilic polymer.

Brief Summary Text - BSTX (6):

From the standpoint of suppressing elution of the added hydrophilic polymer, for example, Japanese Unexamined Patent Publication (Kokai) Nos. 63-97205 and 4-300636 disclose a technique of subjecting a **polysulfone**-base **membrane** having added thereto a hydrophilic polymer such as polyvinylpyrrolidone, to heat treatment or radiation treatment. However, the heat treatment must be performed at a fairly high temperature (170.degree. C. or more) and the **membrane** performance is difficult to maintain. Further, the method of effecting cross-linking by high-power .gamma.-ray irradiation or the like may reduce the blood compatibility of the **membrane**. Furthermore, these methods cannot overcome the problem accompanying the elution of the hydrophilic polymer into the coagulating solution.

Brief Summary Text - BSTX (7):

In order to improve the water permeability of the **polysulfone membrane,** a hydrophilic polymer having low solubility in water may be added. In this respect, a method for forming a **membrane** comprising adding a graft **copolymer** or block **copolymer** consisting of a **polysulfone** segment and a hydrophilic polymer segment is disclosed, for example, in Japanese Unexamined Patent Publication (Kokai) Nos. 62-168503, 62-199621, 62-201603, 63-88003, 63-84603 and 2-140234.

Brief Summary Text - BSTX (9):

An object of the present invention is to provide a **polysulfone**-base hemocatharsis **membrane** having excellent compatibility with the blood.

Brief Summary Text - BSTX (10):

Another object of the present invention is to provide a process for producing a **polysulfone membrane** for purification of blood having excellent compatibility with the blood through a simple washing step with a high recovery of the solvent used for the dope of the formed **membrane**.

Brief Summary Text - BSTX (12):

The present invention has been accomplished by taking advantage of the fact that a **polysulfone membrane** containing a graft **copolymer** and/or block **copolymer** consisting of a hydrophilic segment and a hydrophobic segment exhibits excellent compatibility with the blood and the graft **copolymer** and/or block **copolymer** is not easily eluted into the coagulating solution at the time of forming the **membrane**.

Brief Summary Text - BSTX (13):

More specifically, the objects of the present invention have been attained by a **polysulfone membrane** for purifying blood comprising a graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic segment (exclusive of **polysulfone**), the monomer unit ratio (A/B) of A to B being from 0.5 to 5 and the total of A and B being from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone**.

Brief Summary Text - BSTX (14):

The monomer unit A or B as used herein means a repeating unit in a polymer constituting the hydrophilic segment or the hydrophobic segment, respectively. For example, in a graft or block **copolymer** consisting of a polyvinylpyrrolidone segment and a polystyrene segment, the monomer units A and B are a repeating unit represented by the following formulae [I] and [II], respectively: ##STR1##

Brief Summary Text - BSTX (15):

By analysis of the **membrane** surface, it was found that an improved eluting property and excellent compatibility with blood of the **polysulfone membrane** for purifying blood of the present invention are attained by making the hydrophobic segment embedded in the **polysulfone membrane,** or bonded thereto by a bonding force of the affinity using a graft and/or block **copolymer** comprising the hydrophilic and the hydrophobic segments, whereby the ratio of the hydrophobic segment to the hydrophilic

segment on the **membrane** surface becomes smaller than the ratio of the hydrophobic segment to the hydrophilic segment in the entire **membrane**.

Brief Summary Text - BSTX (16):

More specifically, the present invention further provides a **polysulfone membrane** for purifying blood comprising a graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic

Brief Summary Text - BSTX (17):

segment (exclusive of **polysulfone**), the monomer unit ratio (A/B) of A to B being from 0.5 to 5, the total of A and B being from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** and the monomer unit ratio (U=B'/A') between the hydrophobic segment (B') and the hydrophilic segment (A') present on the surface of the **membrane** being smaller than the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane**.

Brief Summary Text - BSTX (18):

The monomer unit ratio "U" as used herein is defined as a value derived from abundance ratios of the hydrophilic unit in the **copolymer,** the hydrophobic unit in the **copolymer and the polysulfone,** obtained by determining the quantities of characteristic elements of both units and **polysulfone,** elements in the characteristic chemical bonding state (if desired, quantity determined by the peak split process) and the constituent elements according to the ESCA (electron spectroscopy for chemical analysis). For example, a method for determining the monomer unit ratio "U" in the case of a **membrane of polysulfone** resin comprising a repeating unit represented by the following formula [IV] containing a **copolymer** consisting of a polyvinylpyrrolidone segment and a polystyrene segment is described. Abundance ratios of nitrogen originated from the vinylpyrrolidone unit and sulfur originated from **polysulfone** are determined by ESCA. Similarly, the abundance ratio of nitrogen in the polyvinylpyrrolidone film and the abundance ratio of sulfur in the additive-free **polysulfone membrane** are determined by ESCA. From the abundance ratios determined, the covering ratio of the vinylpyrrolidone unit and the exposure ratio of **polysulfone** are determined. Then, from the covering ratio of the vinylpyrrolidone unit and the exposure ratio of **polysulfone,** the covering ratio of the styrene unit is determined. From the covering ratio of the vinylpyrrolidone unit and the covering ratio of the styrene unit, the monomer unit ratio "U" of the **membrane** is obtained.

Brief Summary Text - BSTX (19):

The **polysulfone** as used in the present invention is a polyaryl ether sulfone polymer characterized by the structure containing a repeating unit represented by the following formula [III]. Examples thereof include a polymer comprising a repeating unit represented by formula [IV] and a polymer comprising a repeating unit represented by formula [III]. ##STR2##

Brief Summary Text - BSTX (20):

The graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic segment (exclusive of **polysulfone**) as used in the present invention means a block **copolymer** having a form of A--B, A--B--A, B--A--B, (A--B).sub.X --A, B--(A--B).sub.X, a graft **copolymer** comprising a main chain of (A) a hydrophilic segment and a branch of (B) a hydrophobic segment, or a graft **copolymer** comprising a trunk of (B) a hydrophobic segment and a branch of (A) a hydrophilic segment.

Brief Summary Text - BSTX (21):

The **copolymer** preferably has a molecular weight of from 3.times.10.sup.4 to 2.times.10.sup.6 daltons.

Brief Summary Text - BSTX (22):

Examples of the hydrophilic segment of the present invention include a segment comprising a polymer or **copolymer** of a monomer such as methacrylic acid, acrylic acid, itaconic acid, 2-hydroxyethyl methacrylate, 2-hydroxyethyl **acrylate,** 2-hydroxypropyl methacrylate, 2-hydroxypropyl **acrylate,** glycerol methacrylate, polyethylene glycol methacrylate, N,N'-dimethylacrylamide, N-methylacrylamide, dimethylaminoethyl methacrylate, methylenebisacrylamide, diacetone acrylamide, N-**vinylpyrrolidone** or vinyl alcohol, or a polymer such as a polyethylene glycol segment or a polypropylene glycol segment.

Brief Summary Text - BSTX (23):

Examples of the hydrophobic segment of the present invention include a segment comprising a polymer or **copolymer** of a methacrylic ester or acrylic ester monomer such as methyl methacrylate, ethyl methacrylate, n-propyl methacrylate, n-butyl methacrylate or benzyl methacrylate, a styrene monomer such as styrene, methylstyrene or ethylstyrene, a vinyl carboxylate monomer such as vinyl acetate, or an acrylonitrile monomer.

Brief Summary Text - BSTX (24):

The **copolymer** may be polymerized by a commonly known method. For example, a block **copolymer** may be synthesized from a hydrophilic monomer and a hydrophobic monomer by anionic living polymerization, cationic living polymerization or photoiniferter polymerization (see Nippon Gomu Kyokaishi (Journal of Japan Rubber Association), Vol. 59, No. 12, p. 658 (1986)). The synthesis method of the graft **copolymer** is described, for example, in Japanese Unexamined Patent Publication (Kokai) No. 50-77526 and Angew Makromol. Chem., Vol. 132, 81 (1985). Several Synthesis examples are described below in greater detail. A synthesis example of a block-type **copolymer** by the photoiniferter polymerization is described below. A hydrophilic monomer or a hydrophobic monomer and a living photopolymerization initiator having a dithiocarbamate group (e.g., benzyl N,N-diethyldithiocarbamate, p-xylenebis(N,N-diethyldithiocarbamate)) is dissolved in a solvent and polymerized by irradiating with UV light to synthesize a polymer having a growing terminal. From this reaction solution, the polymer having a growing terminal is purification-separated. This polymer and a hydrophobic monomer in the case of a polymer obtained from a hydrophilic monomer, or a hydrophilic monomer in the case of a polymer obtained from a hydrophobic monomer, are dissolved in a solvent and polymerized starting from the growing terminal by again irradiating with UV light to obtain a block **copolymer**. A block **copolymer** having a repeating unit of (A--B).sub.X --A or (B--A).sub.X --B can be obtained by repeating the purification-separation of the polymer having a growing terminal and the polymerization with a monomer under irradiation with UV light.

Brief Summary Text - BSTX (25):

An example of a synthesis of a block-type **copolymer** by anionic living polymerization is described below. A dehydrated hydrophilic monomer or hydrophobic monomer is polymerized with a polymerization initiator (e.g., sodium naphthalene) in a dehydrated solvent to synthesize a polymer having a growing terminal. After the reaction of the monomer is completed, a dehydrated hydrophobic monomer in the case of a polymer obtained from a hydrophilic monomer, or a dehydrated hydrophilic monomer in the case of a polymer obtained from a hydrophobic monomer, is added to the reaction solution obtained above to effect polymerization starting from the growing terminal. As a result, a block **copolymer** is obtained. A block **copolymer** having a repeating unit of (A--B).sub.X --A or (B--A).sub.X --B can be obtained by repeating the addition of a monomer after completion of the monomer reaction.

Brief Summary Text - BSTX (26):

A synthesis example of a graft-type **copolymer** by the copolymerization of a macromonomer and a monomer is described below. Macromonomers such as polyethylene glycol or polystyrene having a double bond at one terminal are commercially available but the macromonomer can be synthesized by the following

method, if desired. A hydrophilic monomer or hydrophobic monomer is polymerized using azobisisobutyro-nitrile (AIBN) as a polymerization initiator and 3-mercaptopropionic acid as a chain transfer agent to synthesize a prepolymer having a carboxyl group at one terminal. The prepolymer obtained is reacted with glycidyl methacrylate and, as a result, a hydrophilic macromer or hydrophobic macromer is obtained. Other than this, the macromonomer may also be obtained by a method of polymerizing a hydrophilic monomer or hydrophobic monomer by anionic polymerization and adding methacrylic acid chloride thereto to react with the polymer to obtain a hydrophilic macromer or hydrophobic macromer having a double bond at one terminal.

Brief Summary Text - BSTX (27):

A hydrophilic macromer and a hydrophobic monomer or a hydrophobic macromer and a hydrophilic monomer are polymerized in the presence of a polymerization initiator and a graft **copolymer** consisting of a hydrophobic segment and a hydrophilic segment is obtained.

Brief Summary Text - BSTX (28):

The **polysulfone**-base hemocatharsis **membrane** of the present invention can be prepared by a so-called wet film formation process where **polysulfone** and a graft **copolymer** and/or block **copolymer** comprising (A) a hydrophilic segment and (B) a hydrophobic segment in a total amount of from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** with the monomer unit ratio (A/B) between the segments A and B being from 0.5 to 5, is dissolved in a predetermined solvent to have a **polysulfone** concentration of from 12 to 25 wt % based on the prepared dope, the thus-prepared dope for forming a **membrane** is formed into a plane **membrane** or a hollow fiber, the plane **membrane** or hollow fiber formed is contacted with a predetermined coagulating solution, the solvent is removed and the residue is washed.

Brief Summary Text - BSTX (29):

The **polysulfone membrane** for purifying blood of the present invention is advantageous in that the **membrane** having the above-described structure is formed during the coagulation process and the graft **copolymer** and/or block **copolymer** is substantially not eluted into the coagulating solution or the washing solution after the coagulation. Accordingly, in recovering a solvent of the **membrane** from the coagulating solution by distillation or the like, an increase in the viscosity ascribable to elution of the polymer does not occur and a high recovery of the solvent can be achieved. Further, since the polymer is not eluted during washing after the coagulation, the washing step can be completed within a short time.

Brief Summary Text - BSTX (31):

In the graft **copolymer** and/or block **copolymer** for use in the present invention, the hydrophilic segment (A) is preferably a polyvinylpyrrolidone segment or a polyethylene glycol segment, more preferably a polyvinylpyrrolidone segment. The hydrophobic segment (B) is preferably a polymethyl methacrylate segment or a polystyrene segment, more preferably a polystyrene segment.

Brief Summary Text - BSTX (32):

A graft **copolymer** is preferably used. The graft **copolymer** is preferably a graft **copolymer** having a trunk of polymethyl methacrylate segment or polystyrene segment and a branch of polyethylene glycol segment, or a graft **copolymer** having a trunk of polyvinylpyrrolidone segment and a branch of polymethyl methacrylate segment or polystyrene segment, and most preferably a graft polymer having a trunk of polyvinylpyrrolidone and a branch of polystyrene segment.

Brief Summary Text - BSTX (33):

These graft **copolymers** and/or block **copolymers** can be easily prepared by a known synthesis method described in detail above.

Brief Summary Text - BSTX (34):

The **copolymer** preferably has a molecular weight of from 3.times.10.sup.4 to 2.times.10.sup.6 daltons, more preferably from 5.times.10.sup.4 to 1.5.times.10.sup.6 daltons, still more preferably from 1.times.10.sup.5 to 1.times.10.sup.6 daltons. If the molecular weight is too small, satisfactory effects cannot be obtained by addition or the problem of cumbersomeness in the water washing step still remains, whereas if the molecular weight is too large, mixing with the **polysulfone** resin proceeds poorly and a uniform **membrane** cannot be obtained in practice. The molecular weight as used herein means a molecular weight at peak out of the molecular weight in terms of styrene obtained by the gel permeation chromatography (GPC). More specifically, it is a GPC molecular weight at peak in terms of styrene, obtained using a Shodex (trademark) GPC KD-800 series as a column, N,N-dimethylformamide containing 0.01 mol/l of lithium bromide as an eluent and a differential refractometer as a detector.

Brief Summary Text - BSTX (35):

The ratio of the hydrophilic segment (A) to the hydrophobic segment (B) of the present invention is, in terms of the monomer unit ratio (A/B) of A to B, from 0.5 to 5, preferably from 1 to 4, more preferably from 1.2 to 3. The ratio of the hydrophilic segment to the hydrophobic segment is chosen so as to strike a balance between the

insolubility in water and the improvement in the blood compatibility of the **polysulfone**-base **membrane**. More specifically, in the case where the ratio of the hydrophilic segment to the hydrophobic segment is too large, the problem of cumbersomeness in the water washing step is not overcome or the elution into the coagulating solution cannot be sufficiently suppressed, as a result, the recovery of the solvent can be difficult. On the other hand, if the ratio of the hydrophilic segment to the hydrophobic segment is too small, the blood compatibility of the **polysulfone membrane** cannot be sufficiently improved.

Brief Summary Text - BSTX (36):

The hydrophilic segment (A) and the hydrophobic segment (B) each must be contained in the **polysulfone**-base **membrane** of the present invention in an amount such that the total amount of A and B is from 0.5 to 30 parts by weight, preferably from 3 to 25 parts by weight, more preferably from 6 to 20 parts by weight, per 100 parts by weight of **polysulfone**. If the amount of the hydrophilic segment and the hydrophobic segment contained in the **membrane** is too large, there arises a problem in the heat resistance or the mechanical strength of the **membrane**. On the other hand, if the content of these segments are too small, good compatibility with the blood cannot attained.

Brief Summary Text - BSTX (37):

The **polysulfone membrane** for purifying blood of the present invention preferably has a form such that in the cross-sectional structure, the monomer unit ratio (U=B'/A') between the hydrophobic segment (B') and the hydrophilic segment (A') present on the **membrane** surface is smaller than the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane**. For example, when a value (W, decrement of the hydrophobic segment on the **membrane** surface) obtained in such a manner that the monomer unit ratio (U=B'/A') between the hydrophobic segment (B') and the hydrophilic segment (A') present on the **membrane** surface is subtracted from the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane** and the result is divided by the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane,** is used as an index, the index value is preferably from 0.3 to 1, more preferably from 0.5 to 1, still more preferably from 0.7 to 1.

Brief Summary Text - BSTX (38):

The **polysulfone**-base hemocatharsis **membrane** of the present invention can be obtained by a wet film formation process which is a conventionally and commonly known technique. Either a so-called hollow fiber **membrane** having a hollow fiber form or a plane **membrane** may be used. The dope (stock solution for forming a **membrane**)

for use in the wet film formation is a solution obtained by dissolving and mixing the **polysulfone and the copolymer** described above in a solvent which dissolves both the **polysulfone and the copolymer**. The solvent is not particularly limited, however, solvents such as N,N-dimethylacetamide, N,N-dimethylformamide, N-ethyl-pyrrolidone and dimethylsulfoxide have a high solubility and are easily available and therefore, these may be conveniently used. Among these solvents, N,N-dimethylacetaide is most preferred in view of solubility for **polysulfone,** safety to the organism and cost. These solvents may of course be used individually but may be used in combination of two or more solvents so as to adjust the solubility for the polymer.

Brief Summary Text - BSTX (39):

With respect to the concentration of **polysulfone,** if it is too small, the **membrane** can be formed only with difficulty and the strength of the **membrane** may be lowered, whereas if it is too large, the spinning property may be worsened or the hole size may be reduced. Accordingly, the concentration of **polysulfone** is preferably from 12 to 25 wt %, more preferably from 15 to 20 wt %, still more preferably from 16 to 18 wt %, based on the dope. However, the concentration of **polysulfone** is not limited to this range and a concentration lower or higher than this range may be used so as to obtain a **membrane** having desired properties.

Brief Summary Text - BSTX (40):

The **copolymer** added to the dope is scarcely eluted into the coagulation bath during the film formation and therefore, the eluted amount need not be taken into consideration. The **copolymer** may be added in an amount corresponding to the amount of the **copolymer** intended to be present in the **membrane**.

Brief Summary Text - BSTX (41):

The plane **membrane** can be obtained by casting the above-described dope on a substrate such as glass plate by means of a surgical blade and then dipping it in a coagulation bath. The hollow fiber **membrane** can be obtained by extruding the dope from the sheath part of a spinneret of tube-in-orifice type, extruding at the same time an inner coagulating solution from the core part and, after traveling in air, dipping the fibers in a coagulation bath. The inner coagulating solution and the coagulation bath solution for use in the film formation each comprise mainly a solvent, such as water or an alcohol, in which **polysulfone and the copolymer** are only slightly soluble. However, in order to obtain the described properties of the hollow fiber **membrane,** a mixed solution of a solvent of **polysulfone and the copolymer** with water or an alcohol may be used. The plane **membrane** or hollow fiber after dipping in a coagulation bath is, if desired, further washed with water in a water washing bath. The solvent remaining in the **membrane** after the wash may be removed by

Brief Summary Text - BSTX (42):

washing the **membrane** with hot water or the like. Thereafter, the **membrane** may be dried after attaching thereto a hole size retaining agent such as glycerine, if desired.

Brief Summary Text - BSTX (43):

The amount of the hydrophilic segment or the hydrophobic segment contained in the **polysulfone**-base **membrane** may be analyzed by NMR (nuclear magnetic resonance spectroscopic method), for example, from a proton NMR spectrum obtained using a solvent capable of dissolving or thoroughly swelling the **membrane**. For example, in the case of a **polysulfone membrane** comprising a repeating unit represented by formula [IV] containing a **copolymer** consisting of a polyvinylpyrrolidone segment and a polystyrene segment, in the case where chloroform-d.sub.1 is used as a solvent in the analysis, the quantities of **polysulfone,** polyvinylpyrrolidone segment and polystyrene segment can be relatively determined from the peaks in the spectrum when the chemical shift is in the vicinity of 7.85 (4 protons), 3.2 (2 protons) and/or 3.7 (1 proton), and 6.55 (2 protons), respectively. These quantities each can be converted into the part by weight using the formula weight per unit. In the case where the system is complicated and difficult to analyze, fractions divided by the gel permeation chromatography (GPC) or liquid chromatography (LC) may be analyzed one after another by NMR.

Brief Summary Text - BSTX (44):

In analyzing the composition of the dope for forming a **membrane,** low molecular weight substances such as a solvent are removed by evaporation or the like, the polymer obtained is ground into a powder and in the case of containing the hydrophilic polymer and/or hydrophobic homopolymer, these are removed by washing or reprecipitation, and then the residue is dried to obtain a sample polymer composition. The finally obtained polymer composition can be analyzed as described above using NMR. After fractionating the polymer composition by GPC or LC the composition may also be analyzed by subjecting each fraction to NMR analysis or quantitative analysis.

Detailed Description Text - DETX (3):

(1) Quantitative Evaluation of Platelets Adhered (plane **membrane**)

Detailed Description Text - DETX (4):

Whole blood was sampled from a healthy man using a syringe previously containing 3.8 wt % of a sodium citrate solution (1 to 9 volume ratio of blood) and a platelet-rich plasma was prepared by centrifugal separation. Heparin (final concentration: 10 U/ml) and a calcium chloride solution (final concentration: 5 mM) were added to the plasma

and the resulting plasma was contacted with a plane **membrane** and allowed to stand at 37.degree. C. for 1 hour. Thereafter, the **membrane** was washed with phosphoric acid-buffered physiological saline and then, a phosphoric acid-buffered physiological saline solution containing 0.5% of tritonX-100 was added to dissolve the adhered platelets. The lactic acid dehydrogenase activity in the solution obtained was measured by an LDH measurement kit (manufactured by Boelinger Manheim) and the change (.DELTA.ABS) in the absorbance was quantitatively evaluated. The value obtained and converted into a unit area equivalence (unit: IU/m.sup.2) was used as an index for the quantity of platelet adhered.

Detailed Description Text - DETX (8):

The coagulation bath solution used in the formation of a **membrane** and the hot water used in the washing of the **membrane** were combined and subjected to superfractionation under reduced pressure using a fractionating column until the viscosity of the solution amount to 500 pma.cndot.s (measuring temperature: 25.degree. C.) to recover the solvent used in the dope and the coagulating solution. From the amount of solvent recovered and the amount of solvent used (sum of the amount of the solvent in the dope used and the amount of the solvent in the coagulating solution used), the solvent recovery (%) was obtained.

Detailed Description Text - DETX (9):

(4) Quantitative Determination of Additives in **Membrane**

Detailed Description Text - DETX (10):

The **membrane** was thoroughly dried and then dissolved in chloroform-d.sub.1 and the NMR of the solution obtained was measured. The quantities of **polysulfone,** polyvinylpyrrolidone segment and polystyrene segment were relatively determined from the peaks in the spectrum when the chemical shift was in the vicinity of 7.85 (4 protons), 3.2 and 3.7 (3 protons in total), and 6.55 (2 protons), respectively. These quantities each was converted into the part by weight using the formula weight per unit. The monomer unit ratio A/B of (A) polyvinylpyrrolidone segment to (B) polystyrene segment was obtained by the relative determination values.

Detailed Description Text - DETX (11):

(5) Quantitative Determination of **Membrane** Surface Composition

Detailed Description Text - DETX (12):

The **membrane** was thoroughly dried and the abundance ratios of nitrogen originated from vinylpyrrolidone unit and sulfur originated from **polysulfone** polymer on the **membrane** surface were determined by ESCA (electron spectroscopy for chemical analysis). Similarly, the abundance ratio of nitrogen in the polyvinylpyrrolidone **membrane** and the abundance ratio of sulfur in the additive-free **polysulfone membrane** were determined by ESCA. From the abundance ratios determined, the covering ratio (X %) of the vinylpyrrolidone unit and the exposure ratio (Y %) of **polysulfone on the membrane** surface were determined according to the following equations (1) and (2).

Detailed Description Text - DETX (13):

(6) Decrement of Hydrophobic Segment on the **Membrane** Surface

Detailed Description Text - DETX (14):

From the exposure ratio (Y %) of **polysulfone** and the covering ratio (X %) of vinylpyrrolidone unit obtained by the method described in the evaluation method (5), the monomer unit ratio (U=B'/A') between the styrene unit (B') and the vinylpyrrolidone unit (A') present on the **membrane** surface was determined according to the following equation (3). Further, the monomer unit ratio (V=B/A) between the styrene unit (B) and the vinylpyrrolidone unit (A) present in the entire **membrane** was determined by the method described in the evaluation method (4). And, according to the following equation (4), a value obtained by subtracting the monomer unit ratio (U=B'/A') between the styrene unit (B') and the vinylpyrrolidone unit (A') present on the **membrane** surface from the monomer unit ratio (V=B/A) between the styrene unit (B) and the vinylpyrrolidone unit (A) present in the entire **membrane** was divided by the monomer unit ratio (V=B/A) between the styrene unit (B) and the vinylpyrrolidone unit (A) present in the entire **membrane** to obtain a value (W, decrement of the hydrophobic segment on the **membrane** surface).

Detailed Description Text - DETX (17):

The mixed solution in the ampule was heated in a constant-temperature water bath at 60.degree. C. for 8 hours to effect polymerization. From the resulting solution, the solvent was removed under heating in a vacuum and the solid matter obtained was ground into fine powder. The fine powder obtained was washed with cyclohexane in a Soxhlet's extractor, dried and then washed with methanol in a Soxhlet's extractor to remove unreacted styrene macromer, by-produced polyvinylpyrrolidone and the like by extraction. The residue was thoroughly dried in a vacuum drier to obtain a graft polymer as white fine powder. The graft polymer obtained had a monomer unit ratio (A/B) of (A) polyvinylpyrrolidone segment to (B) polystyrene segment of 2.3 and a GPC molecular weight at peak of 2.1.times.10.sup.5 daltons. Subsequently, a dope comprising 18 parts

by weight of **polysulfone** (UDEL P-1700 (trademark), produced by Teijin Acomo Engineering Plastics KK) comprising a repeating unit represented by formula [VI] and 79 parts by weight of N,N-dimethylacetamide per 3 parts by weight of the graft **copolymer** obtained above was prepared. The dope obtained was cast on a glass plate by means of a surgical blade, dipped in a water bath adjusted at a temperature of 40.degree. C. to effect phase separation and then washed three times with hot water at 70.degree. C. for 1 hour by exchanging the hot water. As a result, Plane **Membrane** A was obtained. Plane **Membrane** A was subjected to the quantitative evaluation of platelets adhered and the result is shown in Table 1 as a relative value to the lactic acid dehydrogenase activity per the **membrane** unit area, which is an index for the quantity of platelets adhered to the **polysulfone membrane,** in Comparative Example 1 taken as 100. The amount of the graft **copolymer** remaining in the **membrane** and calculated from the graft **copolymer** content of the plane **membrane** determined by the NMR analysis and the amount of the graft **copolymer** added to the dope, is also shown in Table 1 together with the graft **copolymer** composition (A/B) in the **membrane**. Further, the **membrane** surface composition (the exposure ratio of **polysulfone** polymer and the covering ratio of vinylpyrrolidone unit) determined by the ESCA is shown in Table 6 and the decrement of the hydrophobic segment on the **membrane** surface determined by the ESCA and NMR analysis is shown in Table 7.

Detailed Description Text - DETX (19):

Plane **Membrane** B was manufactured in the same manner as in Example 1 except for using a dope composition comprising 1 part by weight of the graft **copolymer,** 18 parts by weight of **polysulfone** and 81 parts by weight of N,N-dimethylacetamide. Plane **Membrane** B was evaluated on the quantity of platelet adhered, the residual amount of graft **copolymer,** the graft **copolymer** composition in the **membrane, the membrane** surface composition and the decrement of the hydrophobic segment on the **membrane** surface in the same as in Example 1. The results obtained are shown in Tables 1, 6 and 7.

Detailed Description Text - DETX (21):

Plane **Membrane** C was manufactured in the same manner as in Example 1 except for not using the graft **copolymer** and using a dope composition comprising 18 parts by weight of **polysulfone** and 82 parts by weight of N,N-dimethylacetamide. Plane **Membrane** C was evaluated on the quantity of platelet adhered, and the lactic acid dehydrogenase activity per the unit **membrane** area obtained was taken as 100.

Detailed Description Text - DETX (23):

Plane **Membrane** D was manufactured in the same manner as in Example 2 except for using a dope composition comprising 1 part by weight of polyvinylpyrrolidone (K-90, produced by ISP Japan KK), 18 parts by weight of **polysulfone** and 81 parts by weight of

N,N-dimethylacetamide. The quantity of platelet adhered was evaluated in the same manner as in Example 1 and the amount of polyvinylpyrrolidone remaining in the **membrane** was valuated by NMR in the same manner as in Example 1. The results are shown in Table 1.

Detailed Description Text - DETX (25):

Plane **Membrane** E was manufactured in the same manner as in Example 2 except for using a dope composition comprising 5 parts by weight of polyvinylpyrrolidone (K-90), 18 parts by weight of **polysulfone** and 77 parts by weight of N,N-dimethylacetamide. The quantity of platelets adhered was evaluated in the same manner as in Example 1 and the amount of polyvinylpyrrolidone remaining in the **membrane** was measured by NMR in the same manner as in Example 1. The results are shown in Table 1.

Detailed Description Text - DETX (27):

A graft **copolymer** was prepared in the same manner as in Example 1 except for using 13 parts by weight of styrene macromonomer, 87 parts by weight of N-vinylpyrrolidone and 0.15 parts by weight of azobisisobutyronitrile. The graft **copolymer** obtained had a monomer unit ratio (A/B) of (A) polyvinylpyrrolidone segment to (B) polystyrene segment of 2.5 and a GPC molecular weight at peak of 3.8.times.10.sup.5 daltons. Subsequently, a hollow fiber was spun, using this graft **copolymer,** as follows. A dope comprising 18 parts by weight of **polysulfone** (UDEL P-1700) and 79 parts by weight of N,N-dimethylacetamide per 3 parts by weight of the graft **copolymer** obtained above was prepared. The dope was spun into a hollow fiber having an inner diameter of 200 .mu.m and an outer diameter of 290 .mu.m using a 40% N,N-dimethylacetamide aqueous solution as the inner coagulating solution and water as the outer coagulating solution. Hollow Fiber A sampled immediately after taking it out from the coagulation bath was washed eight times with hot water at 90.degree. C. for 20 minutes. A hollow fiber was sampled after every washing and the amount of graft **copolymer** remaining in the hollow fiber was determined by NMR in the same manner as in Example 1. The result obtained is shown in Table 2.

Detailed Description Text - DETX (30):

A hollow fiber was spun in the same manner as in Example 3 except for using a dope comprising 5 parts by weight of polyvinylpyrrolidone (K-90), 18 parts by weight of **polysulfone** and 77 parts by weight of N,N-dimethylacetamide. Hollow Fiber B sampled immediately after taking it out from the coagulation bath was determined on the amount of polyvinylpyrrolidone remaining in the hollow fiber at the washing process in the same manner as in Example 3. The result is shown in Table 2.

Detailed Description Text - DETX (33):

A hollow fiber (Hollow Fiber A') after hot water washing (90.degree. C., 20 minutes, 8 times) of Hollow Fiber A obtained in Example 3 was evaluated on the quantity of platelets adhered. A relative value to the lactic acid dehydrogenase activity per the unit area, which is an index for the quantity of platelets adhered to the **polysulfone** hollow fiber, in Comparative Example 5 taken as 100 is shown in Table 4.

Detailed Description Text - DETX (35):

A hollow fiber (Hollow Fiber C) was spun in the same manner as in Example 3 except for using a dope comprising 1 part by weight of polyvinylpyrrolidone (K-90), 18 parts by weight of **polysulfone** and 81 parts by weight of N,N-dimethylacetamide. Hollow Fiber C after hot water washing (90.degree. C., 20 minutes, 8 times) was evaluated on the quantity of platelets adhered and the lactic acid dehydrogenase activity per the unit area on the inner surface of Hollow Fiber C was taken as 100.

Detailed Description Text - DETX (37):

A hollow fiber (Hollow Fiber D) was spun in the same manner as in Example 3 except for using a dope comprising 1 part by weight of the graft **copolymer,** 18 parts by weight of **polysulfone** and 81 parts by weight of

Detailed Description Text - DETX (38):

N,N-dimethylacetamide. Hollow Fiber D after hot water washing (90.degree. C., 20 minutes, 8 times) was evaluated on the quantity of platelet adhered. A relative value to the lactic acid dehydrogenase activity per the unit area, which is an index for the quantity of platelet adhered to the **polysulfone** hollow fiber, in Comparative Example 5 taken as 100 is shown in Table 4.

Detailed Description Text - DETX (40):

A graft **copolymer** was prepared in the same manner as in Example 1 except for using 20 parts by weight of styrene macromonomer, 80 parts by weight of N-vinylpyrrolidone and 0.10 parts by weight of azobisisobutyronitrile. The graft **copolymer** obtained had a monomer unit ratio (A/B) of (A) polyvinylpyrrolidone segment to (B) polystyrene segment of 1.8 and a GPC molecular weight at peak of 7.9.times.10.sup.5 daltons. Subsequently, a dope comprising 18 parts by weight of **polysulfone** (UDEL P-1700) and 79 parts by weight of N,N-dimethylacetamide per 3 parts by weight of the graft **copolymer** obtained above was prepared. The dope obtained was cast on a glass plate by means of a surgical blade, dipped in a water bath adjusted at a temperature of 40.degree. C. to effect phase separation and then washed three times with hot water at 70.degree. C. for 1 hour by exchanging the hot water. As a result, Plane **Membrane** F was obtained. Plane **Membrane** F was subjected to the quantitative evaluation of platelets adhered. A

relative value of the lactic acid dehydrogenase activity per the **membrane** unit area, which is an index for the quantity of platelet adhered to the **polysulfone membrane,** in Comparative Example 6 taken as 100, and the graft **copolymer** content (parts by weight) of the plane **membrane** per 100 parts by weight of **polysulfone** determined by the NMR analysis are shown in Table 5.

Detailed Description Text - DETX (42):

Plane **Membrane** G was manufactured in the same manner as in Example 6 except for using a dope comprising 1 part by weight of the graft **copolymer,** 18 parts by weight of **polysulfone** and 81 parts by weight of N,N-dimethylacetamide. The lactic acid dehydrogenase activity and the graft **copolymer** content determined in the same manner as in Example 6 are shown in Table 5.

Detailed Description Text - DETX (44):

Plane **Membrane** H was manufactured in the same manner as in Example 6 except for using a dope comprising 0.5 parts by weight of the graft **copolymer,** 18 parts by weight of **polysulfone** and 81.5 parts by weight of N,N-dimethylacetamide. The lactic acid dehydrogenase activity and the graft **copolymer** content determined in the same manner as in Example 6 are shown in Table 5.

Detailed Description Text - DETX (46):

Plane **Membrane** I was manufactured in the same manner as in Example 6 except for using a dope comprising 0.2 parts by weight of graft **copolymer,** 18 parts by weight of **polysulfone** and 81.8 parts by weight of N,N-dimethylacetamide. The lactic acid dehydrogenase activity and the graft **copolymer** content determined in the same manner as in Example 6 are shown in Table 5.

Detailed Description Text - DETX (48):

100 parts of dehydrated styrene and 500 parts of dehydrated tetrahydrofuran were charged in a flask and, thereto, 1.4 parts of 1.6 mol/l.cndot.n-butyl lithium was added while keeping the temperature at -20.degree. C. with stirring in a nitrogen atmosphere. After continuing stirring for 8 hours, the reaction solution was transferred to a flask containing dry ice and stirred. Thereafter, the solution was poured into a large amount of a methanol solution of hydrochloric acid and then a white precipitate was obtained. The precipitate was separated by filtration, washed with water and dried under heating in a vacuum to obtain a styrene polymer having a carboxyl terminal group as white solid matter. 40 parts by weight of the white solid matter obtained, 60 parts by weight of polyvinylpyrrolidone (K-60, ISP Japan KK), 0.2 parts by weight of dimethylaminopyridine and 400 parts by weight of purified chloroform were placed in a

flask and dissolution-mixed under stirring. Thereto, 0.25 parts by weight of dicyclohexyl-carbodiimide was added and the mixed solution was stirred for 6 hours. From the resulting solution, the solvent was removed under heating in a vacuum and then a white solid matter was obtained. This solid matter was grained into fine powder. The fine powder obtained was washed with toluene in a Soxhlet's extractor, dried and then washed with methanol in a Soxhlet's extractor. Thereafter, the fine powder was thoroughly dried in a vacuum drier to obtain a block **copolymer** as white fine powder. The block **copolymer** obtained had a monomer unit ratio (A/B) of (A) polyvinylpyrrolidone segment to (B) polystyrene segment of 2.2 and a GPC peak top molecular weight of 270,000 daltons. Subsequently, Plane **Membrane** J was manufactured in the same manner as in Example 6 except for using a dope comprising 18 parts by weight of **polysulfone** (UDEL P-1700) and 81 parts by weight of N,N-dimethylacetamide per 1 part by weight of the block **copolymer** obtained above. The lactic acid dehydrogenase activity and the block **copolymer** content determined in the same manner as in Example 6 are shown in Table 5.

Detailed Description Text - DETX (50):

Plane **Membrane** C obtained in Comparative Example 1 was evaluated on the quantity of platelet adhered simultaneously with the plane **membranes** obtained in Example 6 to 9. The lactic acid dehydrogenase activity per the unit **membrane** area determined for Plane **Membrane** C was taken as 100.

Detailed Description Text - DETX (52):

A graft **copolymer** was prepared in the same manner as in Example 1 except for using 40 parts by weight of styrene polymer, 60 parts by weight of N-vinylpyrrolidone and 0.25 parts by weight of azobisisobutyronitrile. The graft **copolymer** obtained had a monomer unit ratio (A/B) of (A) polyvinylpyrrolidone segment to (B) polystyrene segment of 0.9 and a GPC molecular weight at peak of 2.5.times.10.sup.5 daltons. Subsequently, a dope comprising 18 parts by weight of **polysulfone** (UDEL P-1700) and 81.5 parts by weight of N,N-dimethylacetamide per 0.5 parts by weight of the graft **copolymer** obtained above was prepared. The dope obtained was cast on a glass plate by means of a surgical blade, dipped in a water bath adjusted at a temperature of 40.degree. C. to effect phase separation and then washed three times with hot water at 70.degree. C. for 1 hour by exchanging the hot water. As a result, Plane **Membrane** K was obtained. Plane **Membrane** K was evaluated on the **membrane** surface composition and the decrement of the hydrophobic segment on the **membrane** surface in the same manner as in Example 1. The results are shown in Tables 6 and 7.

Detailed Description Text - DETX (54):

An N-vinylpyrrolidone-styrene random **copolymer** emulsion (ANTARA430, produced by ISP) was concentrated and dried to solidify. As a result, N-vinylpyrrolidone-styrene random **copolymer** was obtained. Then, Plane **Membrane** L was manufactured in the same manner as in Example 2 except for using a dope comprising 18 parts by weight of **polysulfone** (UDEL P-1700) and 81 parts by weight of N,N-dimethylacetamide per 1 part by weight of the random **copolymer** obtained above. Plane **Membrane** L was evaluated on the **membrane** surface composition and the decrement of the hydrophobic segment on the **membrane** surface in the same manner as in Example 1. The results are shown in Tables 6 and 7.

Detailed Description Text - DETX (58):

The amount of graft **copolymer** and the amount of block **copolymer** are the parts by weight of the graft **copolymer** and the parts by weight of the block **copolymer,** respectively, when the amount of **polysulfone** in the plane **membrane** is taken as 100 parts by weight.

Detailed Description Text - DETX (60):

The **polysulfone membrane** for blood purification of the present invention has excellent compatibility with the blood in methods and is useful as a **membrane** for purifying blood such as hemodialysis and hemofiltration.

Detailed Description Text - DETX (61):

The **polysulfone membrane** for purifying blood of the present invention uses a hydrophobic graft **copolymer** and/or block **copolymer** containing an appropriate amount of a hydrophobic component within the molecule as an additive compatible with the blood and therefore, the additive has strong affinity for the **polysulfone** resin and is not easily eluted even when the **membrane** is contacted with washing water, water for priming or the like.

Detailed Description Text - DETX (62):

Due to this, the **membrane** of the present invention can be produced by a process simplified in the water washing step and elevated in the solvent recovery efficiency. Further, the **membrane** can be produced by a process which dispenses with the work for preventing elution of the polymer, such as cross-linking treatment.

Detailed Description Paragraph Equation - DEEQ (1):

Covering ratio (X %) of vinylpyrrolidone unit=(abundance ratio of nitrogen on the **membrane** surface/abundance ratio of nitrogen in the polyvinylpyrrolidone film).times.100(%) Equation (1):

Detailed Description Paragraph Equation - DEEQ (2):

Exposure ratio (Y %) of **polysulfone**=(abundance ratio of sulfur on the **membrane** surface/abundance ratio of sulfur in the additive-free **polysulfone membrane**).times.100(%) Equation (2):

Detailed Description Paragraph Table - DETL (1):

TABLE 1 _____ Ratio of Quantity of **Copolymer** Platelets Remaining in **Membrane** Adhered **Membrane** (%) A/B _____ Example 1 Plane 23 .+. 6 96 2.3 **Membrane** A Example 2 Plane 36 .+. 16 97 2.4 **Membrane** B Comparative Plane 100 .+. 29 -- -- Example 1 **Membrane** C Comparative Plane 51 .+. 19 48 -- Example 2 **Membrane** D Comparative Plane 27 .+. 12 45 -- Example 3 **Membrane** E

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Detailed Description Paragraph Table - DETL (2):

TABLE 2 _____ Ratio of **Copolymer** Remaining in **Membrane** (%) Number of Times Example 3 Comparative Example 4 of Washing (Hollow Fiber A) (Hollow Fiber B) _____ 0 96 62 1 97 51 2 97 47 3 96 45 4 98 44 5 96 46 6 96 45 7 97 45 8 96 45 _____

Detailed Description Paragraph Table - DETL (5):

TABLE 5 _____ Quantity of Amount of Graft Platelets **Copolymer** or Amount **Membrane** Adhered of Block **Copolymer** _____ Example 6 Plane 10 .+. 3 16 parts by weight **Membrane** F Example 7 Plane 27 .+. 8 5.3 parts by weight **Membrane** G Example 8 Plane 56 .+. 16 2.7 parts by weight **Membrane** H Example 9 Plane 50 .+. 3 1.1 parts by weight **Membrane** I Example 10 Plane 31 .+. 7 5.4 parts by weight **Membrane** J Comparative Plane 100 .+. 9 0 part by weight Example 10 **Membrane** C

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Detailed Description Paragraph Table - DETL (6):

TABLE 6 _____ Covering Ratio (X) of Vinylpyrrolidone Exposure Ratio (Y) Unit (%) of **Polysulfone** (%)

Example 1 43.2 56.3 Example 2 34.5 64.3 Example 11 18.2 73.7 Comparative 15.5 49.0 Example 7

Detailed Description Paragraph Table - DETL (7):

TABLE 7 Decrement of Hydrophobic Segment on the **Membrane** Surface

Example 1 0.97 Example 2 0.92 Example 11 0.60 Comparative Example 7 0.02

Claims Text - CLTX (1):

1. A **polysulfone membrane** for purifying blood comprising a **polysulfone** and a graft **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic segment, the monomer unit ratio (A/B) of (A) to (B) being from 0.5 to 5 and the total of (A) and (B) being from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** wherein (B) is not **polysulfone,** and wherein (A) the hydrophilic segment and (B) the hydrophobic segment form the graft **copolymer**.

Claims Text - CLTX (2):

2. The **polysulfone membrane** for purifying blood as claimed in claim 1, wherein (A) a hydrophilic segment and (B) a hydrophobic segment form the block **copolymer**.

Claims Text - CLTX (3):

3. A **polysulfone membrane** for purifying blood comprising a **polysulfone** and a graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic segment, the monomer unit ratio (A/B) of (A) to (B) being from 0.5 to 5 and the total of (A) and (B) being from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** wherein (B) is not **polysulfone,** and wherein (B) the hydrophobic segment is a polystyrene segment.

Claims Text - CLTX (4):

4. The **polysulfone membrane** for purifying blood as claimed in claim 3, wherein the hydrophilic segment is a polyvinylpyrrolidone segment.

Claims Text - CLTX (5):

5. A **polysulfone membrane** for purifying blood comprising a **polysulfone** and a graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a

hydrophobic segment, the monomer unit ratio (A/B) of (A) to (B) being from 0.5 to 5 and wherein the total of the hydrophilic segment (A) and the hydrophobic segment (B) is from 6 to 20 parts by weight per 100 parts by weight of **polysulfone,** wherein (B) is not **polysulfone**.

Claims Text - CLTX (6):

6. The **polysulfone membrane** for purifying blood as claimed in claim 5, wherein the monomer unit ratio (A/B) of the hydrophilic segment (A) to the hydrophobic segment (B) is from 1 to 4.

Claims Text - CLTX (7):

7. The **polysulfone membrane** for purifying blood as claimed in claim 5, wherein the monomer unit ratio (A/B) of the hydrophilic segment (A) to the hydrophobic segment (B) is from 1.2 to 3.

Claims Text - CLTX (8):

8. A process for producing a **polysulfone membrane** for purifying blood, comprising dissolving polysulfonc and a graft **copolymer** comprising (A) a hydrophilic segment and (B) a hydrophobic segment in a total amount of from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** with the monomer unit ratio (A/B) between the segments (A) and (B) being from 0.5 to 5, in a predetermined solvent to have a **polysulfone** concentration of from 12 to 25 wt % based on the dope prepared, forming the film formation dope into a plane **membrane** or a hollow fiber, contacting the plane **membrane** or hollow fiber formed with a predetermined coagulating solution, removing the solvent and washing the residue; wherein (B) is not **polysulfone,** and (A) the hydrophilic segment and (B) the hydrophobic segment form the graft **copolymer**.

Claims Text - CLTX (9):

9. The process for producing a **polysulfone membrane** for purifying blood as claimed in claim 8, wherein the hydrophilic segment is a polyvinylpyrrolidone segment and the hydrophobic segment is a polystyrene segment.

Claims Text - CLTX (10):

10. A **polysulfone membrane** for purifying blood comprising a **polysulfone** and a graft **copolymer** and/or block **copolymer** consisting of (A) a hydrophilic segment and (B) a hydrophobic segment, the monomer unit ratio (A/B) of (A) to (B) being from 0.5 to 5 and the total of (A) and (B) being from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** wherein (B) is not a **polysulfone,** and wherein the monomer unit

ratio (U=B'/A') between the hydrophobic segment (B') and the hydrophilic segment (A') present on the surface of the **membrane** is smaller than the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane**.

Claims Text - CLTX (11):

11. The **polysulfone membrane** for purifying blood as claimed in claim 10, wherein the value (W) obtained by dividing a value resulting from subtracting the monomer unit ratio (U=B'/A') between the hydrophobic segment (B') and the hydrophilic segment (A') present on the **membrane** surface from the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane,** by the monomer unit ratio (V=B/A) between the hydrophobic segment (B) and the hydrophilic segment (A) present in the entire **membrane** is from 0.3 to 1.

Claims Text - CLTX (12):

12. A process for producing a **polysulfone membrane** for purifying blood comprising dissolving **polysulfone** and a graft **copolymer** and/or block **copolymer** comprising (A) a hydrophilic segment and (B) a hydrophobic segment in a total amount of from 0.5 to 30 parts by weight per 100 parts by weight of **polysulfone,** with the monomer unit ratio (A/B) between the segments (A) and (B) being from 0.5 to 5, in a predetermined solvent to have a **polysulfone** at a concentration of from 12 to 25 wt % based on the dope prepared, forming the film formation dope into a plane **membrane** or a hollow fiber, contacting the plane **membrane** or hollow fiber formed with a predetermined coagulating solution, removing the solvent and washing the residue; wherein (B) is not **polysulfone,** and (B) the hydrophobic segment is a polystyrene segment.

Claims Text - CLTX (13):

13. The process for producing a **polysulfone membrane** for purifying blood as claimed in claim 12, wherein (A) a hydrophilic segment and (B) a hydrophobic segment form the block **copolymer**.

Claims Text - CLTX (14):

14. The process for producing a **polysulfone membrane** for purifying blood as claimed in claim 12, the hydrophilic segment is a polyvinylpyrrolidone segment.

Current US Original Classification - CCOR (1):

210/500.41